

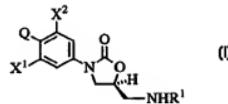


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(71) Applicant (for all designated States except US): PHARMACIA & UPJOHN COMPANY [US/US]; 301 Henrietta Street, Kalamazoo, MI 49001 (US).	
(72) Inventors; and	Published
(75) Inventors/Applicants (for US only): THOMASCO, Lisa, Marie [US/US]; 953 Dobbins Drive, Kalamazoo, MI 49006 (US), GADWOOD, Robert, C. [US/US]; 5232 Stonchenge Drive, Kalamazoo, MI 49008 (US). ANDERSON, David, J. [GB/US]; 3809 Middlebury Drive, Kalamazoo, MI 49006 (US).	With international search report.
(74) Agent: YANG, Lucy, X.; Pharmacia & Upjohn Company, Intellectual Property Legal Services, 301 Henrietta Street, Kalamazoo, MI 49001 (US).	

(54) Title: THIADIAZOLYL AND OXADIAZOLYL PHENYL OXAZOLIDINONE ANTIBACTERIAL AGENTS



(57) Abstract

The present invention provides thiadiazolyl and oxadiazolyl phenyl oxazolidinone compounds of formula (I) wherein Q is thiadiazolyl or oxadiazolyl; wherein X¹ and X² are independently hydrogen, fluorine, or chlorine; and wherein R¹ is, for example, -COCH₃ or -COCH₂CH₃. These compounds are useful antimicrobial agents, effective against a number of human and veterinary pathogens, including gram-positive and gram-negative aerobic bacteria.

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THIADIAZOLYL AND OXADIAZOLYL PHENYL OXAZOLIDINONE
ANTIBACTERIAL AGENTS

BACKGROUND OF THE INVENTION

5 The subject invention discloses thiadiazolyl and oxadiazolyl phenyl oxazolidinone derivatives. The compounds are useful antimicrobial agents, effective against a number of human and veterinary pathogens, including gram-positive aerobic bacteria such as multiply-resistant staphylococci, streptococci and enterococci, as well as anaerobic organisms such as *Bacteroides spp.*, and acid-fast organisms such as *Mycobacterium tuberculosis*.

10

Piperazine-containing oxazolidinones are disclosed in International Publication No. WO93/23384, November 25, 1987 (PCT/US93/03570). International Publication No. WO95/14684, June 1, 1995 (PCT/US94/10582) discloses esters of the oxazolidinone, piperazine ring structures disclosed in the above PCT application.

15 International Publication No. WO95/07271, March 16, 1995 (PCT/US94/08904) discloses oxazolidinones although containing morpholine and thiomorpholine instead of the subject piperazine.

20 Other earlier publications in the area of oxazolidinones are US Patent Nos. 4,801,600; 4,921,869; EPA 0352781 (January 31, 1989); and EPA 0316594 (May 24, 1989) all assigned to E.I. DuPont De Nemours and Company, which are cited here to exemplify the state of the art.

INFORMATION DISCLOSURE

25 International Publication No. WO 93/09103, published 13 May 1993, and corresponding US Patent No. 5,565,571, disclose substituted aryl- and heteroarylphenyl-oxazolidinones useful as antibacterial agents. Among the heteroaryl groups disclosed are groups such as imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl and triazolyl.

30 International Publication No. WO96/23788, published 8 August 1996, discloses nitrogen-containing heteroaromatic ring substituted phenyloxazolidinone antimicrobials. This 5-member nitrogen-containing hetero-aromatic ring has from 1 to 4 nitrogen atoms and is attached to the phenyloxazolidinone through one of the nitrogen atoms.

US Patent Nos. 4,948,801; 5,043,443; 5,130,316; and 5,254,577 aminomethyloxooxazolidinyl aryl-substituted benzene derivatives useful as antibacterial

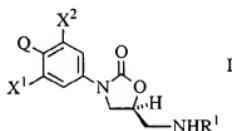
agents. Among the aromatic groups disclosed are groups such as diazinyl, triazinyl, thiazolyl, oxazolyl and unsubstituted 1,2,3-thiadiazol-4-yl. These compounds do not have flanking halogens on the benzene ring.

International Publication No. WO97/30981, published 28 August 1997, discloses 5 azolyl piperazinyl phenyl oxazolidinone antibacterials. Among the five-membered ring heterocycles (i.e., azolyl rings) disclosed are groups such as thiadiazolyl, oxadiazolyl, thiazolyl, benzothiazolyl, thiatriazolyl, imidazolyl, benzimidazolyl, triazolyl, tetrazolyl, pyrazolyl, pyrazolyl, indazolyl, benzoisothiazolyl, isoxazolyl and benisoxazolyl. In all cases, the piperazine nitrogen atom is attached at the carbon atom of the carbon-nitrogen 10 double bond of the heterocyclic ring.

US Serial No. 09/080,751, filed 18 May 1998 discloses oxazolidinone antibacterial agents having a thiocarbonyl functionality. It discloses the compound (S)-N-[(3-[3-fluoro-4-[4-(5-methyl-1,3,4-thiadiazol-2-yl)-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl)methyl]thioacetamide.

15 **SUMMARY OF THE INVENTION**

The present invention provides a compound of structural formula I:



or a pharmaceutically acceptable salt thereof.

wherein R¹ is

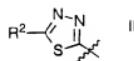
20 (a) -COR³,
 (b) -COCH₂Cl,
 (c) -COCHCl₂,
 (d) -COCH₂F,
 (e) -COCHF₂,
 25 (f) -CO₂CH₃,
 (g) -SO₂CH₃,
 (h) -COCH₂OH,
 (i) -CSR³,
 (j) -CSNH₂, or

(k) $-\text{CSNHCH}_2-$:

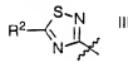
X^1 and X^2 are independently H, F, or Cl; and Q is an optionally substituted five membered ring heterocycle incorporating two nitrogen atoms and one sulfur or oxygen atom.

5 More specifically, in the present invention, Q is:

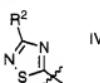
(a) 1,3,4-thiadiazol-2-yl:



(b) 1,2,4-thiadiazol-3-yl:



(c) 1,2,4-thiadiazol-5-yl:



15 (d) 1,2,5-thiadiazol-3-yl:

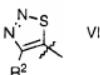


(e) 1,2,3-thiadiazol-4-yl:

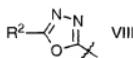


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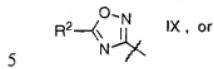
(f) 1,2,3-thiadiazol-5-yl:



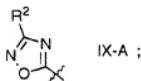
(g) 1,3,4-oxadiazol-2-yl:



(h) 1,2,4-oxadiazol-3-yl:



(i) 1,2,4-oxadiazol-5-yl

10 wherein R^2 is

- (a) R^3-
- (b) $R^4CO_2(CH_2)_n-$,
- (c) $NC(CH_2)_n-$,
- (d) $R^3OCO(CH_2)_n-$,
- 15 (e) $R^3R^5NCO(CH_2)_n-$,
- (f) $R^3R^5N(CH_2)_n-$,
- (g) $R^4CONR^5(CH_2)_n-$,
- (h) $CF_3(CH_2)_n-$,
- (i) $CF_2H(CH_2)_n-$,
- 20 (j) $R^4CO(CH_2)_n-$,
- (k) $F(CH_2)_n-$,
- (l) $Cl(CH_2)_n-$,
- (m) $Br(CH_2)_n-$,
- (n) $R^3O(CH_2)_n-$,
- 25 (o) $R^3S(CH_2)_n-$,
- (p) $R^3SO(CH_2)_n-$,
- (q) $R^3SO_2(CH_2)_n-$,
- (r) $R^3SO_2NR^5(CH_2)_n-$,

- (s) $R^3R^4C(OH)(CH_2)_n-$,
- (t) $R^3R^4C(NHR^5)(CH_2)_n-$,
- (u) $HO_2C(CH_2)_n-$,
- (v) $O_2N(CH_2)_n-$,
- 5 (w) C_2-C_6 alkenyl,
- (x) C_2-C_6 alkynyl,
- (y) $-CCl_3$,
- (z) $R^3ON=CR^3(CH_2)_n-$,
- (aa) $NCNR^5(CH_2)_n-$,
- 10 (bb) $R^3ONR^5(CH_2)_n-$, or
- (cc) $R^3OC(O)NR^5(CH_2)_n-$;

wherein n is 0, 1, 2, 3, 4 or 5;

wherein p is 1, 2 or 3;

wherein R^3 is

- 15 (a) H,
- (b) C_1-C_5 alkyl, or
- (c) cyclopropyl-;

wherein R^4 is

- (a) H,
- 20 (b) C_1-C_5 alkyl-,
- (c) cyclopropyl-,
- (d) $R^3O(CH_2)_p-$, or
- (e) $R^3CO_2(CH_2)_p-$;

wherein R^5 is

- 25 (a) H, or
- (b) C_1-C_3 alkyl;

or a pharmaceutically acceptable salt thereof;

with the following proviso:

at least one of X^1 and X^2 is F or Cl.

- 30 More specifically, the present invention provides a compound of formula I
- wherein R^1 is $-COR^3$, or $-CSR^3$;
- wherein X^1 and X^2 are independently

- (a) H, or

(b) F;

wherein Q is the moiety of formula II or IV;

wherein R² is

- (a) R³,
- 5 (b) R⁴CO₂(CH₂)_n-,
- (c) NC(CH₂)_n-,
- (d) R³OCO(CH₂)_n-,
- (e) R³R⁵NCO(CH₂)_n-,
- (f) R³R⁵N(CH₂)_n-,
- 10 (g) R⁴CONR⁵(CH₂)_n-,
- (h) CF₃(CH₂)_n-,
- (i) R⁴CO(CH₂)_n-,
- (j) F(CH₂)_n-,
- (k) Cl(CH₂)_n-,
- 15 (l) R³O(CH₂)_n-,
- (m) R³S(CH₂)_n-,
- (n) R³SO(CH₂)_n-,
- (o) R³SO₂(CH₂)_n-,
- (p) R³SO₂NR⁵(CH₂)_n-,
- 20 (q) O₂N(CH₂)_n-, or
- (r) R³R⁴C(NHR⁵)(CH₂)_n-,

wherein n is 0, 1, or 2;

wherein R⁴ is

- (a) H,
- 25 (b) C₁-C₃ alkyl, or
- (c) cyclopropyl.

Even more specifically, the present invention provides the compound of formula I wherein R² is

- (a) R³,
- 30 (b) NC(CH₂)_n-,
- (c) R³NHCO(CH₂)_n-,
- (d) R⁴CO(CH₂)_n-,
- (e) F(CH₂)_n-,

- (g) $\text{Cl}(\text{CH}_2)_n^-$,
- (h) $\text{R}^3\text{O}(\text{CH}_2)_n^-$,
- (i) $\text{R}^3\text{S}(\text{CH}_2)_n^-$,
- (j) $\text{R}^3\text{NH}(\text{CH}_2)_n^-$, or
- 5 (k) $\text{R}^4\text{CONH}(\text{CH}_2)_n^-$.

Even more specifically, the present invention provides the above compounds wherein Q is the moiety of formula II.

In another aspect, the subject invention is directed toward a method for treating microbial infections in patients by administering to a patient in need thereof an effective 10 amount of a compound of Formula I as described above. The compound may be administered in a pharmaceutical composition either orally, parenterally, transdermally, or topically. Preferably, the compound is administered in an amount of from about 0.1 to about 100 mg/kg of body weight/day, more preferably, from about 3.0 to about 50 mg/kg of body weight/day. Some of the compounds of the present invention, especially the 15 1,3,4-thiadiazol-2-yl-containing compounds, are also surprisingly effective antibacterial agents against fastidious gram-negative bacteria/organisms. The activity of several compounds of the present invention against a gram-negative bacterial strain is given in Table 2.

The compounds of the present invention are named according to the IUPAC or 20 CAS nomenclature system.

The carbon atoms content of various hydrocarbon-containing moieties is indicated by a prefix designating the minimum and maximum number of carbon atoms in the moiety; i.e., the prefix $\text{C}_i\text{-}\text{C}_j$ indicates a moiety of the integer "i" to the integer "j" carbon atoms, inclusive. Thus, for example, $\text{C}_1\text{-}\text{C}_3$ alkyl refers to alkyl of one to three carbon 25 atoms, inclusive, or ethyl, ethyl, propyl, and isopropyl.

Examples of alkyl of one to nine carbon atoms, inclusive, are methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, and nonyl, and all isomeric forms thereof, straight and branched.

Examples of alkenyl of one to five carbon atoms, inclusive, are ethenyl, propenyl, 30 butenyl, pentenyl, and all isomeric forms thereof.

DETAILED DESCRIPTION OF THE INVENTION

The X^1 and X^2 groups may be independently either hydrogen atoms or the defined halogen atoms in a variety of substitution patterns. The X^1 and X^2 substituents are preferably one fluorine and one H.

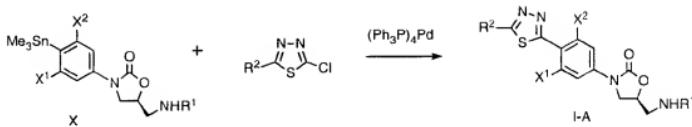
5 The preferred absolute configuration at C-5 of the oxazolidinone ring of compounds claimed in this invention is as represented in the structure of Formula I. This configuration is called (*S*) under the Cahn-Ingold-Prelog nomenclature system. It is this (*S*)-enantiomer which is antibacterially active. The racemic mixture is useful in the same way and for the same purpose as the pure (*S*)-enantiomer; the difference is that twice as 10 much racemic material must be used to produce the same antibacterial effect. It will be apparent to one skilled in the art that selected azolyl ring systems may have additional chiral centers present to give diastereomers. These diastereomers, in racemic and enantiomerically enriched forms, are also within the scope of the compounds of Formula I.

15 As is apparent to those of ordinary skill in the art, the compounds of the present invention can exist in several tautomeric forms, and all such tautomeric forms are included within the scope of the present invention. For instance, in the compound of Example 29 below, the 4,5-dihydro-5-oxo-1,3,4-thiadiazol-2-yl group can exist as the 5-hydroxy-1,3,4-thiadiazol-2-yl group and both such tautomers are included within the 20 scope of the present invention.

Methods for preparing the oxazolidinones of Formula I are depicted in the following pages. It will be apparent to those skilled in the art that the described synthetic procedures are merely representative in nature and that alternative procedures are feasible and may be preferred in some cases.

25 1,3,4-Thiadiazoles (I-A) of the present invention (formula I wherein Q is moiety II) are made by the reaction of the trimethylstannylphenyl oxazolidinone, X, with 2-chloro-1,3,4-thiadiazoles as shown in Scheme I-A below. Oxazolidinone X is prepared as described in US Patent No. 5,565,571 (Preparation 19). The required 2-chloro-1,3,4-thiadiazoles are well known in the chemical literature and many methods exist for their 30 preparation.

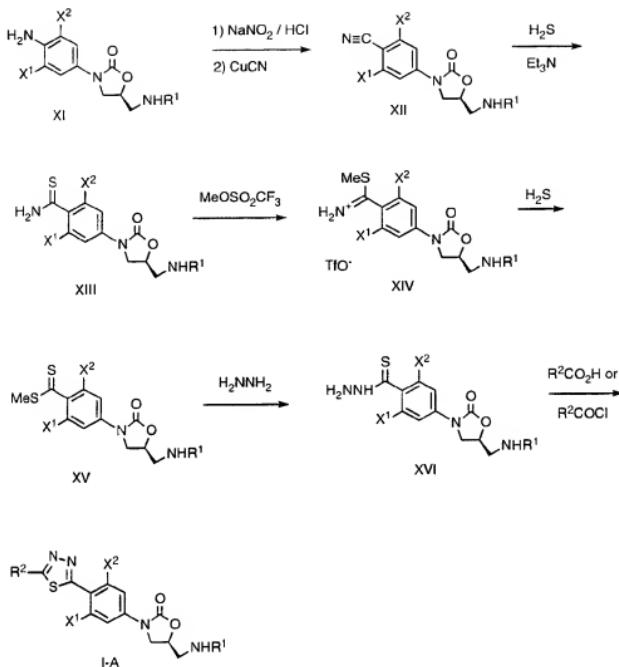
Scheme I-A



5 Alternatively, oxazolidinones I-A are preferably made by the sequence of steps shown in Scheme 1 below. Diazotization of aniline XI (prepared as described in International Publication No. WO 96/23788, published 8 August 1996, on page 33, lines 13-20) and reaction of the diazonium salt with cuprous cyanide gives the nitrile, XII. This nitrile is converted to the thioamide XIII by reaction with hydrogen sulfide.

10 Methylation of the thioamide is carried out by reaction with methyl triflate to produce the isothioamide XIV. Reaction of XIV with hydrogen sulfide gives the dithiobenzoate ester, XV. Addition of hydrazine to XV produces the thiobenzhydrazide XVI. Reaction of XVI with various carboxylic acids or acid chlorides affords the thiadiazoles I-A.

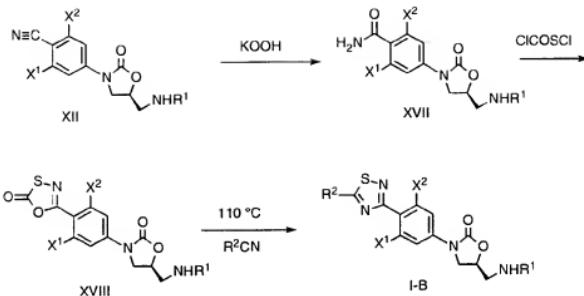
Scheme 1



1,2,4-Thiadiazoles (I-B) of the present invention (formula I wherein Q is moiety III) are made by the reaction sequence shown in Scheme 2 below. Hydrolysis of the nitrile XII to the amide XVII is accomplished with potassium hydroperoxide. Reaction of XVII with chlorocarbonylsulfenylchloride produces the oxathiazolone, XVIII. Pyrolysis of XVIII in the presence of various nitriles leads to oxazolidinones I-B.

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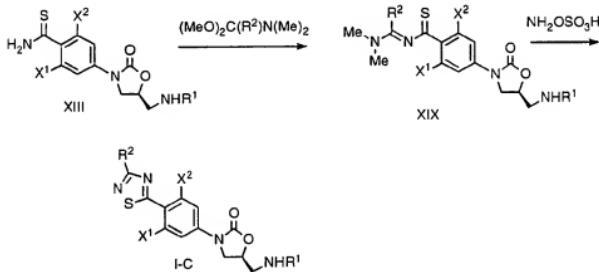
Scheme 2



1,2,4-Thiadiazoles (I-C) of the present invention (formula I wherein Q is moiety IV) are made by procedures outlined by Y. Lin (*J. Org. Chem.* 1980, **45**, 3750-3753) as shown in

5 Scheme 3 below. Thus, reaction of the thiobenzamide XIII with a dimethoxyalkylamine leads to the amidine, XIX. Treatment of this amidine with hydroxylamine sulfonic acid produces the oxazolidinone I-C.

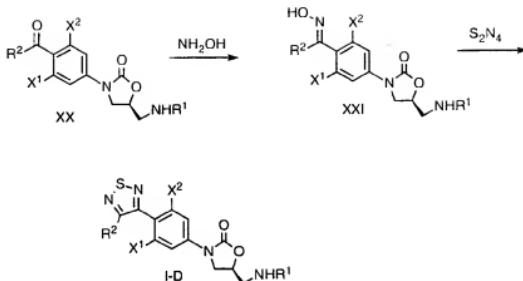
Scheme 3



10 1,2,5-Thiadiazoles (I-D) of the present invention (formula I wherein Q is moiety V) are made by procedures outlined by J. Cho (*J. Chem. Soc. Perkin Trans. I.* 1993, 2345-2350). As shown in Scheme 4 below, reaction of the appropriate aryl ketone XX with hydroxylamine gives the oxime XXI. Treatment of XXI with S2N4 produces oxazolidinone I-D. The required ketones are prepared by procedures disclosed by C-H.

15 Park (*J. Med. Chem.* 1992, **35**, 1156-1165).

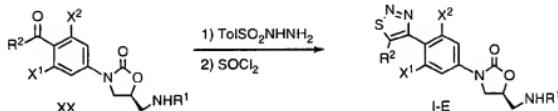
Scheme 4



1,2,3-Thiadiazoles (I-E) of the present invention (formula I wherein Q is moiety VI) are made from the appropriate ketone XX by procedures outlined by E. Thomas (*J. Med.*

5 *Chem.* 1985, 28, 2345-2350) and shown below in Scheme 5.

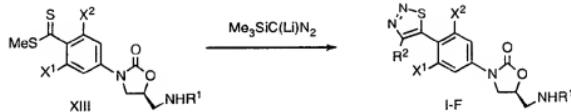
Scheme 5



1,2,3-Thiadiazoles (I-F) of the present invention (formula I wherein Q is moiety VII) are made from the dithiobenzoate XIII according to the method of T. Aoyama (*Heterocycles*,

10 *1986, 24, 589-592*), as shown in Scheme 6 below.

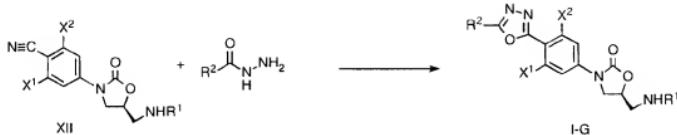
Scheme 6



1,3,4-oxadiazoles (I-G) of the present invention (formula I wherein Q is moiety VIII) are made from the nitrile XII using the appropriate acylhydrazide, following the procedures

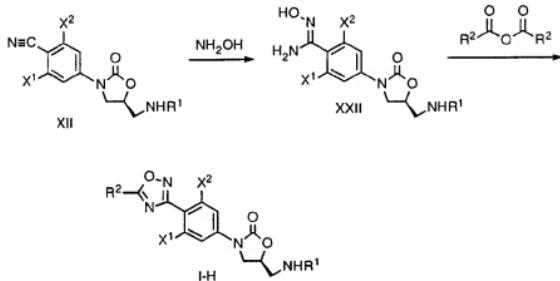
15 reported by R. L. Harris (*Aust.J.Chem.* 1977, 30, 2225-2240) as shown below in Scheme 7.

Scheme 7

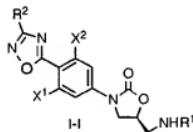


1,2,4-Oxadiazoles (I-H) of the present invention (formula I wherein Q is moiety IX) are
 5 made from the nitrile XII by conversion to the hydroxyamidine XXII and then cyclization with the appropriate anhydride, as shown in Scheme 8 below.

Scheme 8



The 1,2,4-Oxadiazoles (I-I) of the present invention (formula I wherein Q is
 10 moiety IX-A) are made as additional products from the reaction shown in Scheme 3.



The preparation of oxazolidinones having a thiocarbonyl functionality is disclosed
 in US Patent Application, Serial No. 60/048,342, filed 30 May 1997, which is hereby
 15 incorporated by reference herein.

The compounds of Formula I are useful for treatment of microbial infections in humans and other warm blooded animals, under both parenteral, topical, transdermal, and oral administration.

The pharmaceutical compositions of this invention are prepared by combining the compounds of Formula I of this invention with a solid or liquid pharmaceutically acceptable carrier and, optionally, with pharmaceutically acceptable adjuvants and excipients employing standard and conventional techniques. Solid form compositions 5 include powders, tablets, dispersible granules, capsules, cachets and suppositories. A solid carrier can be at least one substance which may also function as a diluent, flavoring agent, solubilizer, lubricant, suspending agent, binder, tablet disintegrating agent, and encapsulating agent. Inert solid carriers include magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, cellulosic materials, low 10 melting wax, cocoa butter, and the like. Liquid form compositions include solutions, suspensions and emulsions. For example, there may be provided solutions of the compounds of this invention dissolved in water and water-propylene glycol and water-polyethylene glycol systems, optionally containing suitable conventional coloring agents, flavoring agents, stabilizers and thickening agents.

15 Preferably, the pharmaceutical composition is provided employing conventional techniques in unit dosage form containing effective or appropriate amounts of the active component, that is, the compound of Formula I according to this invention.

The quantity of active component, that is the compound of Formula I according to this invention, in the pharmaceutical composition and unit dosage form thereof may be 20 varied or adjusted widely depending upon the particular application, the potency of the particular compound and the desired concentration. Generally, the quantity of active component will range between 0.5% to 90% by weight of the composition.

In therapeutic use for treating, or combatting, bacterial infections in warm-blooded animals, the compounds or pharmaceutical compositions thereof will be 25 administered orally, parenterally, transdermally, or topically at a dosage to obtain and maintain a concentration, that is, an amount, or blood-level of active component in the animal undergoing treatment which will be antibacterially effective. The therapeutic uses of these compounds include their use in treating ocular infections and other ophthalmic uses. Generally, such antibacterially effective amount of dosage of active component will 30 be in the range of about 0.1 to about 100, more preferably about 3.0 to about 50 mg/kg of body weight/day. It is to be understood that the dosages may vary depending upon the requirements of the patient, the severity of the bacterial infection being treated, and the particular compound being used. Also, it is to be understood that the initial dosage

administered may be increased beyond the above upper level in order to rapidly achieve the desired blood-level or the initial dosage may be smaller than the optimum and the daily dosage may be progressively increased during the course of treatment depending on the particular situation. If desired, the daily dose may also be divided into multiple doses for administration, e.g., two to four times per day.

The compounds of Formula I according to this invention are administered parenterally, i.e., by injection, for example, by intravenous injection or by other parenteral routes of administration. Pharmaceutical compositions for parenteral administration will generally contain a pharmaceutically acceptable amount of the compound according to

10 Formula I as a soluble salt (acid addition salt or base salt) dissolved in a pharmaceutically acceptable liquid carrier such as, for example, water-for-injection and a buffer to provide a suitably buffered isotonic solution, for example, having a pH of about 3-7. Suitable buffering agents include, for example, trisodium orthophosphate, sodium bicarbonate, sodium citrate, N-methylglucamine, L(+)-lysine and L(+)-arginine to name but a few

15 representative buffering agents. The compound according to Formula I generally will be dissolved in the carrier in an amount sufficient to provide a pharmaceutically acceptable injectable concentration in the range of about 1 mg/ml to about 400 mg/ml of solution. The resulting liquid pharmaceutical composition will be administered so as to obtain the above-mentioned antibacterially effective amount of dosage. The compounds of Formula

20 I according to this invention, due to their aqueous solubility, are advantageously administered orally in solid and liquid dosage forms.

The oxazolidinone antibacterial agents of this invention have useful activity against a variety of microorganisms. The *in vitro* activity of compounds of this invention can be assessed by standard testing procedures such as the determination of minimum

25 inhibitory concentration (MIC) by agar dilution as described in "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically" (MFT) published Jan. 1983 by the National Committee for Clinical Laboratory Standards, 771 East Lancaster Avenue, Villanova, Pennsylvania 19084, USA. The activity of selected compounds of this invention against *Staphylococcus aureus* and *Streptococcus*

30 *pneumoniae* are shown in Table 1.

The following compounds of the present invention are preferred:

1. (*S*)-*N*-{[3-[4-(5-Cyano-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl}acetamide;

2. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-carboxamide;
3. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
5. 4. (*S*)-*N*-[[3-[4-(5-Ethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
5. 5. (*S*)-*N*-[[3-[3-Fluoro-4-(5-propyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
6. 6. (*S*)-*N*-[[3-[4-[5-(Aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 10 7. *S*-*N*-[[3-[3-Fluoro-4-[5-[(methylsulfonyl)amino]methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
8. 8. (*S*)-*N*-[[3-[3-Fluoro-4-(5-fluoromethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 15 9. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
10. 10. (*S*)-*N*-[[3-[4-(5-Acetoxyethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
11. 11. (*S*)-*N*-[[3-[3-Fluoro-4-(5-hydroxymethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 20 12. 12. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methoxymethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
13. 13. (*S*)-*N*-[[3-[4-[5-(Cyanomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 25 14. 14. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-acetamide;
15. 15. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
16. 16. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-oxobutyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 30 17. 17. (*SS*)-*N*-[[3-[3-Fluoro-4-[5-(3-hydroxybutyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

18. (*S*)-Methyl 5-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-propanoate;

19. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-propanamide;

5 20. (*S*)-*N*-[[3-[4-[5-(2-Cyanoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

21. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[(methylthio)methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

22. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[(methylsulfinyl)methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

10 23. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylthio)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

24. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylsulfinyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

15 25. (*S*)-Ethyl 5-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-acetate;

26. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(2-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

27. (*S*)-Ethyl 5-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-carboxylate;

20 28. (55)-*N*-[[3-[3-Fluoro-4-[5-(2-hydroxypropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

29. (*S*)-*N*-[[3-[4-(4-(5-Dihydro-5-oxo-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

25 30. (*S*)-*N*-[[3-[4-(5-Amino-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

31. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylthio)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

32. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

30 33. (*S*)-3-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,2,4-thiadiazole-5-carboxamide;

34. (*S*)-*N*-[[3-[3-Fluoro-4-(1,2,4-thiadiazol-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

35. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

5 36. (*S*)-*N*-[[3-[3-Fluoro-4-(1,2,4-oxadiazol-3-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

37. (*S*)-3-[4-[5-(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,2,4-oxadiazole-5-carboxamide;

38. (*S*)-*N*-[[3-[4-(5-Cyano-1,2,4-oxadiazol-3-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

10 39. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

40. (*S*)-*N*-[[3-[3-Fluoro-4-(1,2,4-oxadiazol-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

15 41. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(formylamino)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

42. (*S*)-*N*-[[3-[4-[5-(2-Chloroethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

20 43. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(1-propenyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

44. (*S*)-*N*-[[3-[4-[5-(2-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

45. (*S*)-*N*-[[3-[4-[5-[2-(Acetylamino)ethyl]-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

25 46. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-[(methylsulfonyl)amino]ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

47. (*SS*)-*N*-[[3-[3-Fluoro-4-[5-(methylsulfinyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

48. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(1-methylethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

30 49. (*S*)-*N*-[[5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide;

50. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-hydroxypropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

51. [*S*-(*R*^{*,*R*^{*})-*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

5 52. [*S*-(*R*^{*,*S*^{*})-*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

53. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(2-nitroethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

54. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-nitropropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

10 55. [*S*-(*R*^{*,*R*^{*})-*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

56. [*S*-(*R*^{*,*S*^{*})-*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

15 57. (*S*)-*N*-[[3-[4-[5-(3-Aminopropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

58. (*S*)-*N*-[3-[5-[4-[5-[(Acetyl)amino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]propyl]acetamide;

59. (*S*)-*N*-[[3-[4-(5-Acetyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

20 60. (*S*)-*N*-[[3-[4-[5-(3-Chloropropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

61. (*S*)-*N*-[[3-[4-[5-(3-Cyanopropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

25 62. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylsulfonyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

63. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[3-(hydroxyimino)butyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

64. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(hydroxyimino)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

30 65. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[3-(methoxyimino)butyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

66. (*S*)-*N*-[5-[4-[5-[(Acetyloxyacetyl)amino]methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide;

67. (*S*)-*N*-[5-[4-[5-[(Hydroxyacetyl)amino]methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide;

5 68. (*S*)-*N*-[5-[4-[5-[(Acetyl)amino]methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]-2-(acetyloxy)acetamide;

69. (*S*)-*N*-[3-[3-Fluoro-4-[5-[(methylsulfonyl)methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

70. (*S*)-*N*-[3-[3-Fluoro-4-[5-[2-(methylsulfonyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

10 71. (*S*)-*N*-[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

72. (*S*)-*N*-[3-[3-Fluoro-4-[5-(2-methoxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

15 73. (*S*)-*N*-[3-[3-Fluoro-4-[5-(2-methoxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

74. (*S*)-*N*-[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]ethanethioamide;

75. (*S*)-[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]thiourea;

20 76. (*S*)-*N*-[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanethioamide;

77. *N*-[(55)-3-[4-[5-(aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl]ethanethioamide;

25 78. 2-((5-(4-((5S)-5-[ethanethioyl]amino)methyl)-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl)-1,3,4-thiadiazol-2-yl)methyl]amino)-2-oxoethyl acetate; and

79. *N*-[5-(4-((5S)-5-[ethanethioyl]amino)methyl)-2-oxo-1,3-oxazolidin-3-yl]-2-fluorophenyl)-1,3,4-thiadiazol-2-yl)methyl]-2-hydroxyacetamide.

The following compounds of the present invention are most preferred:

30 1. (*S*)-*N*-[3-[4-(5-Cyano-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

2. (*S*)-*N*-[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

3. (*S*)-*N*-[[3-[4-(5-Ethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
4. (*S*)-*N*-[[3-[4-[5-(Aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
5. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[(methylsulfonyl)amino]methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
6. (*S*)-*N*-[[3-[3-Fluoro-4-(5-fluoromethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
7. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 10 8. (*S*)-*N*-[[3-[4-(5-Acetoxymethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
9. (*S*)-*N*-[[3-[3-Fluoro-4-(5-hydroxymethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 15 10. (*S*)-*N*-[[3-[4-[5-(Cyanomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
11. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-acetamide;
12. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-oxobutyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 20 13. (*S*)-*N*-[[3-[4-[5-(2-Cyanoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
14. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylsulfinyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 25 15. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(2-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
16. (*S*)-*N*-[[3-[4-(4,5-Dihydro-5-oxo-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
17. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylthio)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 30 18. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

19. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylsulfinyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

20. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-hydroxypropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

5 21. [*S*-(*R*^{*,*R*⁴)-]*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide}

22. [*S*-(*R*^{*,*S*⁴)-]*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

10 23. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(2-nitroethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

24. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-nitropropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

15 25. [*S*-(*R*^{*,*R*⁴)-]*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

26. [*S*-(*R*^{*,*S*⁴)-]*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

27. (*S*)-*N*-[[3-[4-[5-(3-Cyanopropyl)-1,3,4-thiadiazol-2-yl]3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

10 28. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[3-(hydroxyimino)butyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

29. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(hydroxyimino)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

20 30. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylsulfonyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

31. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

32. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]ethanethioamide;

25 33. (*S*)-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]thiourea;

34. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanethioamide;

35. *N*-{[(5S)-3-{4-[5-(aminomethyl)-1,3,4-thiadiazol-2-yl]3-fluorophenyl}-2-ox-1,3-oxazolidin-5-yl)methyl]ethanethioamide;

36. 2-({[5-(4-((5S)-5-[(ethanethioylamino)methyl]-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl)-1,3,4-thiadiazol-2-yl)methyl]amino)-2-oxoethyl acetate; or

5 37. *N*-{[5-(4-((5S)-5-[(ethanethioylamino)methyl]-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl)-1,3,4-thiadiazol-2-yl)methyl}-2-hydroxyacetamide.

Table 1.

In Vitro Activity of Examples Against Selected Gram-Positive Bacteria

Example No.	MIC (µg/mL)	
	<i>S. aureus</i> UC ^b 9213	<i>S. pneumoniae</i> UC ^b 9912
1	0.5	<0.125
2	0.5	0.25
3	1	<0.125
4	1	0.25
5	1	0.25
6	8	<0.125
7	4	<0.125
8	1	0.25
9	1	0.25
10	1	<0.125
11	1	<0.125
12	2	0.25
13	2	0.25
14	4	<0.125
15	2	0.5
16	1	<0.125
17	2	0.25
18	2	0.25
19	8	<0.125
20	0.5	<0.125
21	1	0.25

Example No.	MIC (µg/mL)	
	<i>S. Aureus</i> UC* 9213	<i>S. pneumoniae</i> UC* 9912
22	8	0.25
24	1	0.25
24	4	0.25
25	2	0.25
29	2	<0.125
27	8	<0.125
29	2	0.25
29	1	0.25
30	4	0.25
31	0.5	<0.125
32	1	<0.125
33	16	8
34	1	0.25
35	16	4
36	4	8
37	>16	8
38	>16	2
39	16	8
40	2	0.5
40	4	0.5
42	4	<0.125
43	2	0.5
44	>16	0.25
45	16	0.5
46	16	0.5
47	2	0.25
48	1	0.25
49	16	0.25
50	2	0.25
51	2	0.25

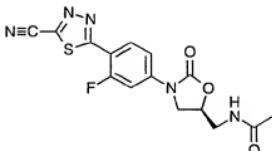
Example No.	MIC (µg/mL)	
	<i>S. Aureus</i> UC [®] 9213	<i>S. pneumoniae</i> UC [®] 9912
52	2	0.25
53	1	0.25
53	2	0.25
55	8	<0.125
56	4	<0.125
57	16	0.5
58	8	0.25
59	2	0.5
60	2	0.5
64	1	<0.125
62	2	0.5
58	2	<0.125
64	1	<0.125
65	8	2
66	16	<0.5
67	16	<0.5
68	8	2
69	4	<0.5
70	4	<0.5
71	1	0.25
72	4	0.25
73	2	<0.5
74	0.25	<0.125
75	0.25	<0.125
76	0.25	<0.125
77	<0.5	<0.5
78	2	<0.5

Table 2.
MIC Data for a Gram Negative Bacterial Strain

Example No.	MIC (μ g/mL) for HI 30063
8	2
8	2
7	4
6	2
7	2
8	4
8	4
10	4
11	4
13	4
14	4
16	4
20	2
24	4
26	2
29	4
31	4
32	4
47	4
50	4
51	4
52	4
53	4
51	4
55	4
56	4
64	4
63	4
64	2
70	4
71	4
74	1
75	1
76	1
77	<0.5
78	4

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Example 1. (*S*)-*N*-{[3-[4-(5-Cyano-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl}acetamide (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CN). Refer to Scheme 1-A.

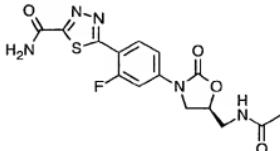


5

A mixture of the oxazolidinone X, prepared as described in US 5,565,571 (Preparation 19) (208.1 mg), 2-chloro-5-cyano-1,3,4-thiadiazole (72.9 mg), tris(dibenzylideneacetone)dipalladium(0) (9.1 mg) and triphenylarsine (12.2 mg) in 1-methyl-2-pyrrolidinone (3 mL) is evacuated and flushed with N₂ three times. The dark 10 reaction mixture is stirred under N₂ for 6 days. The reaction mixture is partitioned between water (20 mL) and ethyl acetate (30 mL) and the phases are separated. The aqueous phase is extracted with ethyl acetate (2 x 25 mL). The combined organics are washed with water (20 mL), brine (20 mL), dried (MgSO₄), filtered and concentrated. The dark residue is purified by flash chromatography using 5% methanol in ethyl acetate 15 as the eluent to afford 25.2 mg of the desired thiadiazole.

Physical characteristics are as follows: mp 210-211 °C. ¹H NMR (DMSO) δ 8.39, 8.24, 7.78, 7.60, 4.78, 4.19, 3.81, 3.43, 1.81; Anal. Found: C, 48.67; H, 3.57; N, 18.86; S, 8.33.

Example 2. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-carboxamide (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = H₂NCO). Refer to Scheme 1.

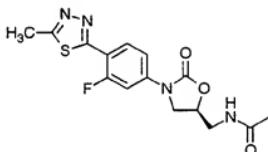


A solution of the title compound of Example 1 (58.6 mg) in 10:1 H₂SO₄ / H₂O (1 mL) is heated at 40 °C for 3.5 h. The cooled reaction mixture is treated with ice (15 mL)

and the mixture is adjusted to pH 7 with 50 % NaOH, resulting in formation of a solid precipitate. The reaction mixture is concentrated. The resulting solid is dissolved in methanol/chloroform, absorbed onto silica gel, and purified on 20 g of silica gel using 8% methanol in dichloromethane as the eluent to afford 37.1 mg of the title product as a tan 5 solid.

Physical characteristics are as follows: mp 243-244 °C (dec). ^1H NMR (DMSO) δ 8.62, 8.32, 8.25, 8.18, 7.76, 7.59, 4.76, 4.18, 3.80, 3.42, 1.81.

Example 3. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{CH}_3$). Refer to Scheme 1.



Step 1. The aniline XI, prepared as described in International Publication No. WO 96/23788, published 8 August 1996 (5.2 g) is dissolved in 2 N HCl (23 mL) and cooled to 0 °C. Sodium nitrite (2.0 g) in water (12 mL) is added and the resulting yellow 15 solution is stirred at 0 °C for 30 min. Solid sodium bicarbonate is carefully added until the solution reaches pH 7. In a separate flask, copper (I) cyanide (2.3 g) and potassium cyanide (1.9 g) are suspended in water (19 mL) and ethyl acetate (38 mL) at 0 °C. The neutralized diazonium salt is added to this solution via cannula over 35 min. The resulting mixture is stirred at 0 °C for 30 min (during which time the mixture becomes 20 very dark in color) then at room temperature for 1 h. The dark heterogeneous reaction mixture is filtered through a pad of celite to remove copper salts. The filter cake is washed with ethyl acetate (2 x 50 mL) and water (1 x 50 mL). The phases of the filtrate are separated. The aqueous layer is extracted with ethyl acetate (100 mL). The combined organics are dried (MgSO_4), filtered and concentrated. The orange residue is dissolved in 25 30% acetone in dichloromethane and filtered through a short column of silica gel using 30% acetone in dichloromethane as the eluent. The filtrate is concentrated to afford 3.4 g of desired nitrile XII as a yellow solid.

Physical characteristics are as follows: mp 173-174 °C. ^1H NMR (DMSO) δ 8.22, 7.92, 7.74, 7.52, 4.76, 4.14, 3.76, 3.40, 1.80. Anal. Found: C, 56.16; H, 4.34; N, 14.83.

Step 2. To a stirred solution of the nitrile XII (prepared in Step 1, 3.06 g) in 30 mL of DMF is added triethylamine (3.8 mL) at room temperature. The reaction is heated to 100 °C and H_2S is bubbled into the flask for 1 h. The reaction is then cooled to 60 °C over 30 min. A portion of the DMF (15 mL) is removed via bulb to bulb distillation. The reaction mixture is then poured onto 100 mL of ice and stirred until the ice melts. The mixture is filtered and the orange solid is dried overnight in a vacuum oven to afford 2.9 g of the thioamide XIII. An analytical sample of the thioamide is prepared by chromatography through a Biotage 40S column (1 % MeOH in CH_2Cl_2).

Physical characteristics are as follows: mp 116-119 °C ; ^1H NMR (DMSO) δ 10.1, 9.4, 8.23, 7.12, 7.46, 7.29, 4.7, 4.12, 3.73, 3.4045, 1.81. Anal. Found: C, 50.54; H, 4.70; N, 13.04; S, 9.60.

Step 3. To a stirred solution of the thioamide XIII (prepared in step 2, 1.05 g) in 1:1 THF/ CH_2Cl_2 (37 mL) under N_2 is added methyl triflate (0.49 mL). The resulting orange solution is stirred at room temperature for 1 h, then pyridine (0.82 mL) is added. Hydrogen sulfide is bubbled through the reaction mixture for 1 h. The hydrogen sulfide is replaced with N_2 and nitrogen is bubbled through the reaction mixture for 30 min. The orange solution is concentrated. The resulting orange residue is dissolved in MeOH/ CH_2Cl_2 , absorbed onto silica, and purified using a Biotage 40 M column with a SIM using 2.5% MeOH in CH_2Cl_2 as the eluent to afford 640.2 mg of the methyl dithiobenzoate XV as an orange foam which is used immediately in the next reaction without further purification.

Physical characteristics are as follows: ^1H NMR (CDCl_3) 7.68, 7.47, 7.13, 6.81, 4.80, 4.04, 3.79, 3.64, 2.73, 2.00.

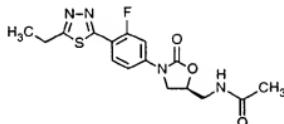
Step 4. To a stirred solution of the dithiobenzoate XV (prepared in step 3, 640.2 mg) in ethanol (18 mL) is added hydrazine monohydrate (0.33 mL). (The orange color of the dithiobenzoate dissipates within 5 min after addition of hydrazine). The reaction mixture is stirred at room temperature for 25 min, then concentrated. The yellow residue is dissolved in methanol/ CH_2Cl_2 , absorbed onto silica, and purified on a Biotage 40S column using a SIM and 7% methanol in dichloromethane as the eluent to afford 369.0 mg (60%) of the desired thiohydrazide XVI.

Physical characteristics are as follows: mp 207-208 °C (bubbles). ^1H NMR (DMSO) δ 12.4, 8.23, 7.54, 7.48, 7.29, 6.25, 4.73, 4.11, 3.72, 3.40, 1.81.

Step 5. To a stirred suspension of the thiohydrazide XVI (prepared as described in step 4, 200.0 mg) in dry THF (4 mL) is added acetyl chloride (52 μL). The reaction mixture is heated at reflux for 30 min, cooled and concentrated. The yellow solid is dissolved in MeOH/CH₂Cl₂, absorbed onto silica, and purified by flash chromatography using 7% methanol in dichloromethane as the eluent to afford 156.7 mg of the desired thiadiazole I-A as an off-white solid.

Physical characteristics are as follows: mp 240-242 °C. ^1H NMR (DMSO) δ 10 8.22, 7.72, 7.53, 4.76, 4.16, 3.78, 3.42, 2.77, 1.81; Anal. Found: C, 51.30; H, 4.17; N, 15.97.

Example 4. (S)-N-[[3-[4-(5-Ethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃CH₂). Refer to Scheme 1.

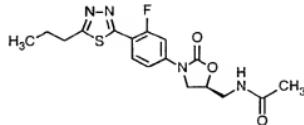


15

The thiohydrazide XVI from Step 4 of Example 3 (200 mg) is reacted with propionyl chloride (107 μL) according to the procedure of Step 5 of Example 3 to afford 261 mg of the title compound.

20 Physical characteristics are as follows: mp 221-223 °C. ^1H -NMR (DMSO) δ 8.23, 7.70, 7.53, 4.76, 4.17, 3.80, 3.42, 3.15, 1.82, 1.35. Anal. Found: C, 52.69; H, 4.59; N, 15.39.

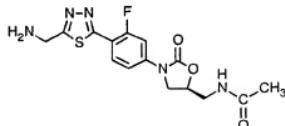
Example 5. (S)-N-[[3-[3-Fluoro-4-(5-propyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = CH₃CH₂CH₂). Refer to Scheme 1.



The thiohydrazide XVI from Step 4 of Example 3 (300 mg) is reacted with butyryl chloride (190 μ L) according to the procedure of Step 5 of Example 3 to afford 205 mg of the title compound.

Physical characteristics are as follows: mp 210-212 $^{\circ}$ C. 1 H-NMR (DMSO) δ 8.24, 5 7.70, 7.53, 4.76, 4.17, 3.80, 3.42, 3.09, 1.82, 1.79, 0.96. Anal. Found: C, 53.57; H, 5.02; N, 14.69.

Example 6. (S)-N-[[3-[4-[5-(Aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X^1 = H, X^2 = F, R^1 = CH_3CO , R^2 = NH_2CH_2). Refer to Scheme 1.



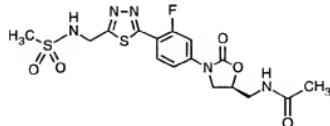
10

Step 1. The thiohydrazide XVI from Step 4 of Example 3 (532 mg) is reacted with Fmoc glycyl chloride (669 mg) according to the procedure of Step 5 of Example 3 to afford 631 mg of the Fmoc protected form of the title compound.

Step 2. The product from step 1 is stirred in 5 mL of piperidine at room temperature for 1 h. The desired product is collected by filtration. The mother liquor is absorbed onto silica gel and chromatographed using 2% MeOH (saturated with NH_3) in CH_2Cl_2 as eluent to afford 178 mg of the title compound.

Physical characteristics are as follows: mp 216-217 $^{\circ}$ C. 1 H-NMR (DMSO) δ 8.22, 7.70, 7.52, 4.76, 4.17, 4.13, 3.80, 3.42, 1.82. % H_2O : 3.65. Anal. Found: C, 46.09; H, 4.45; N, 17.01.

Example 7. (S)-N-[[3-[3-Fluoro-4-[5-[(methylsulfonyl)amino]methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X^1 = H, X^2 = F, R^1 = CH_3CO , R^2 = $CH_3SO_2NHCH_2$). Refer to Scheme 1.



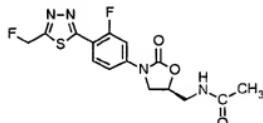
25

To a suspension of the amine prepared in Example 6 (300 mg) in CH_2Cl_2 (10 mL) is added triethylamine (459 μ L) and methanesulfonyl chloride (127 μ L). The reaction is

heated to 100 °C for 2 h. The reaction mixture is then cooled to room temperature and concentrated. The residue is absorbed onto silica gel and chromatographed using 10% MeOH/CH₂Cl₂ as eluent to afford 161 mg of the title compound.

Physical characteristics are as follows: mp 160 °C. ¹H-NMR (DMSO) δ 8.22, 5 7.70, 7.52, 4.77, 4.17, 4.13, 3.81, 3.42, 3.29, 1.82. % H₂O: 3.08. Anal. Found: C, 46.12; H, 4.47; N, 17.06.

Example 8. (S)-N-[(3-[3-Fluoro-4-(5-fluoromethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl)methyl]acetamide (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = FCH₂). Refer to Scheme 1.



10

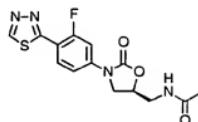
Prepared from the thiohydrazide XVI according to the procedure of Step 5 of Example 3, substituting fluoroacetyl chloride for acetyl chloride. Purified by flash chromatography using 5% methanol in dichloromethane to give 107.0 mg of the desired fluoromethyl thiadiazole as a white solid.

15

Physical characteristics are as follows: mp 222-223 °C. ¹H NMR (DMSO) δ 8.30, 8.27, 7.76, 7.57, 6.01, 5.85, 4.77, 4.18, 3.80, 3.42, 1.81; Anal. Found: C, 48.64; H, 3.90; N, 15.09.

20

Example 9. (S)-N-[(3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl)-methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = H). Refer to Scheme 1.



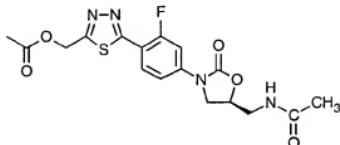
A mixture of thiohydrazide XVI from Step 4 of Example 3 (195 mg) and formic acid (2 mL) is heated at reflux for 45 min. The cooled reaction mixture is concentrated.

25

The resulting residue is dissolved in methanol, absorbed onto silica gel and purified by flash chromatography using 5% MeOH in CH₂Cl₂ to afford 134 mg of the title compound.

Physical characteristics are as follows: mp 234-235 °C. $^1\text{H-NMR}$ (DMSO) δ 9.75, 8.27, 7.75, 7.55, 4.77, 4.17, 3.79, 3.42, 1.81. Anal. Found: C, 49.87; H, 3.79; N, 16.64; S, 9.43.

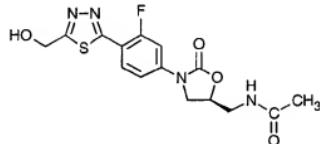
Example 10. (*S*)-*N*-[[3-[4-(5-Acetoxymethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-A, $\text{X}^1 = \text{H}$, $\text{X}^2 = \text{F}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{CH}_3\text{CO}_2\text{CH}_2$). Refer to Scheme 1.



Prepared from the thiohydrazide XVI according to the procedure of Step 5 of Example 3, substituting acetoxyacetyl chloride for acetyl chloride. Purified by flash chromatography using 5% methanol in dichloromethane as the eluent to afford 374.1 mg of the title thiadiazole as an off-white solid.

Physical characteristics are as follows: mp 181-182 °C. $^1\text{H-NMR}$ (DMSO) δ 8.27, 7.75, 7.55, 5.53, 4.76, 4.17, 3.76, 3.42, 2.11, 1.81.

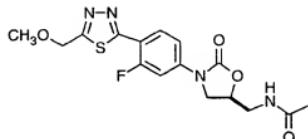
Example 11. (*S*)-*N*-[[3-[3-Fluoro-4-(5-hydroxymethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-A, $\text{X}^1 = \text{H}$, $\text{X}^2 = \text{F}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{HOCH}_2$). Refer to Scheme 1.



Potassium carbonate (60.6 mg) is added to a stirred suspension of the title compound of Example 10 (128.0 mg) in methanol (3 mL). The heterogeneous reaction mixture is stirred at room temperature for 15 min. Dichloromethane (3 mL) is added and the homogenous reaction mixture is filtered through a plug of cotton to remove the solids. The filtrate is absorbed onto silica gel and purified by flash chromatography using 10% methanol in dichloromethane as the eluent to afford 93.6 mg of the desired hydroxymethyl thiadiazole as a white solid.

Physical characteristics as follows: mp 212-214 °C. ^1H NMR (DMSO) δ 8.24, 7.73, 7.54, 6.25, 4.90, 4.77, 4.17, 3.81, 3.42, 1.81; Anal. Found: C, 49.00; H, 4.20; N, 15.23; S, 8.55.

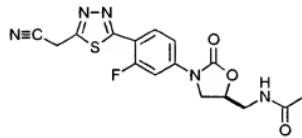
Example 12. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methoxymethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{CH}_3\text{OCH}_2$). Refer to Scheme 1.



The thiohydrazide XVI from Step 4 of Example 3 (343 mg) is reacted with methoxyacetyl chloride (228 mg) according to the procedure of Step 5. Example 3 to afford 339 mg of the title compound.

Physical characteristics are as follows: mp 198-199 °C. ^1H -NMR (DMSO) δ 8.26, 7.73, 7.55, 4.90, 4.77, 4.17, 3.79, 3.42, 3.40, 1.81. % Water (KF) = 0.13. Anal. Found: C, 49.40; H, 4.44; N, 14.39; S, 8.24.

Example 13. (*S*)-*N*-[[3-[4-[5-(Cyanomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{NCCH}_2$). Refer to Scheme 1.



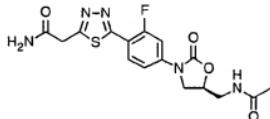
Step 1. To a stirred solution of cyanoacetic acid (10.0 mmol) in CH_2Cl_2 (40 mL) is added oxalyl chloride (11.0 mmol) followed by 2 drops of DMF. The reaction mixture is stirred at RT for 1-18 h, then concentrated. The cyanoacetyl chloride is isolated by distillation.

Step 2. The thiohydrazide XVI of Step 4 of Example 3 (216 mg) is reacted with cyanoacetyl chloride (82 mg) according to the procedure of Step 5 of Example 3 to afford 164 mg of the title compound.

Physical characteristics are as follows: mp 250-251 °C. ¹H-NMR (DMSO) δ 8.26, 7.76, 7.56, 4.75, 4.17, 3.79, 3.42, 1.81. % Water (KF) = 0.65. Anal. Found: C, 50.03; H, 3.91; N, 17.98; S, 8.33.

Example 14. (S)-[4-[5-[(Acetylaminomethyl)-2-oxo-3-oxazolidinyl]-2-

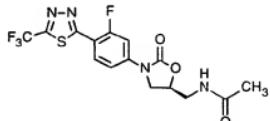
5 fluorophenyl]-1,3,4-thiadiazole-2-acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = H₂NCOCH₂). Refer to Scheme 1.



A solution of the nitrile of Example 13 (378 mg) in 7 mL of 10:1 H₂SO₄/H₂O is 10 heated at 40 °C for 3h. The cooled reaction mixture is poured onto 20 mL of ice and the pH is adjusted to 7 with 50% NaOH. A tan precipitate forms. The solid is isolated by filtration, washing with H₂O and drying. The solid is dissolved in MeOH/CH₂Cl₂, absorbed onto silica gel and purified by flash chromatography using 10% MeOH in CH₂Cl₂ as the eluent to afford 227 mg of the title compound.

15 Physical characteristics are as follows: mp 248-249 °C. ¹H-NMR (DMSO) δ 8.24, 7.81, 7.72, 7.53, 7.31, 4.76, 4.17, 4.09, 3.80, 3.42, 1.81; % Water (KF) = 1.02; Anal. Found: C, 48.35; H, 4.17, N, 17.01, S, 7.80.

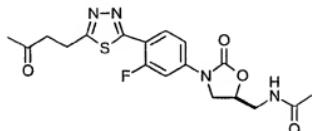
Example 15. (S)-N-[[3-[3-Fluoro-4-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, 20 R² = CF₃). Refer to Scheme 1.



The thiohydrazide XVI from Step 4 of Example 3 (300 mg) is refluxed in neat trifluoroacetic acid (3 mL) for 8 h and then stirred overnight at rt. The reaction mixture is then concentrated in vacuo. The residue is triturated with CH₃CN to afford 156 mg of the 25 title compound.

Physical characteristics are as follows: mp 237-239 °C. ¹H-NMR (DMSO) δ 8.38, 8.26, 7.78, 7.61, 4.78, 4.19, 3.81, 3.43, 1.82. Anal. Found: C, 44.97; H, 3.12; N, 13.90.

Example 16. (S)-N-[[3-[3-Fluoro-4-[5-(3-oxobutyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃COCH₂CH₂). Refer to Scheme 1.

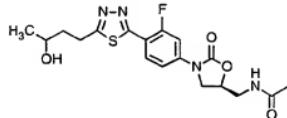


Step 1. Levulinyl chloride is prepared from levulinic acid and oxalyl chloride following the procedure of Step 1, Example 13.

10 Step 2. The thiohydrazide XVI of Step 4 of Example 3 (328 mg) is reacted with levulinyl chloride (268 mg) according to the procedure of Step 5, Example 3 to afford 323 mg of the title compound.

Physical characteristics are as follows: mp 209-210 °C. ¹H-NMR (DMSO) δ 8.23, 7.68, 7.52, 4.76, 4.16, 3.78, 3.42, 3.28, 3.03, 2.13, 1.81. Anal. Found: C, 52.86; H, 4.71; N, 13.79; S, 7.76.

Example 17. (S)-N-[[3-[3-Fluoro-4-[5-(3-hydroxybutyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = CH₃CH(OH)CH₂CH₂). Refer to Scheme 1.

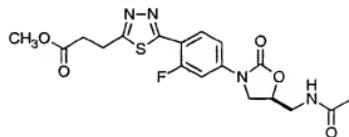


20 To a stirred suspension of the ketone of Example 16 (280 mg) in methanol, cooled to 0 °C, is added sodium borohydride (52 mg). The reaction mixture is stirred at room temperature for 1 h, then additional sodium borohydride (25 mg) is added. Stirring is continued for an additional 3 h, then the reaction mixture is treated with water. The reaction mixture is poured into CH₂Cl₂ (50 mL) and the phases are separated. The aqueous phase is extracted with CH₂Cl₂ (3 x 25 mL) and the combined organic phases are dried (MgSO₄), filtered and concentrated. The residue is dissolved in methanol, absorbed

onto silica gel and purified by flash chromatography using 5% MeOH in CH_2Cl_2 as the eluent to afford 130.3 mg of the title compound as a white solid.

Physical characteristics are as follows: mp 200-201 °C. $^1\text{H-NMR}$ (DMSO) δ 8.23, 7.72, 7.53, 4.76, 4.62, 4.17, 3.78, 3.67, 3.42, 3.16, 1.81, 1.10. Anal. Found: C, 55.59; H, 5.16; N, 13.63; S, 7.78.

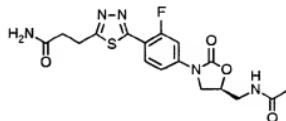
Example 18. (S)-Methyl 5-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-propanoate. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{CH}_3\text{OCOCH}_2\text{CH}_2$). Refer to Scheme 1.



10 The thiohydrazide XVI of Example 3 (346 mg) is reacted with 3-carbomethoxypropionyl chloride (335 mg) according to the procedure of Step 5, Example 3 to afford 327 mg of the title compound.

Physical characteristics are as follows: mp 200-202 °C. $^1\text{H-NMR}$ (DMSO) δ 8.22, 7.70, 7.52, 4.76, 4.17, 3.78, 3.60, 3.40, 2.89, 1.81. Anal. Found: C, 51.06; H, 4.52; N, 13.23; S, 7.42.

Example 19. (S)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-propanamide. (I-A, $\text{X}^1 = \text{H}$, $\text{X}^2 = \text{F}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{NH}_2\text{COCH}_2\text{CH}_2$). Refer to Scheme 1.

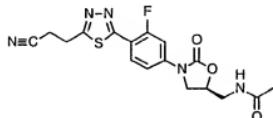


20 The ester of Example 18 (156.7 mg) in methanolic ammonia (7 mL) is heated in a sealed tube at 100 °C for 12 h. A solid precipitate forms upon cooling. The solid is isolated by filtration, washed with ether and dried to afford 115.0 mg of the title compound as a white solid.

Physical characteristics are as follows: mp 254-255 °C. ¹H-NMR (DMSO) δ 8.22, 7.72, 7.53, 7.41, 6.90, 4.76, 4.17, 3.79, 3.42, 2.60, 1.81. Anal. Found: C, 49.71; H, 4.49; N, 17.13; S, 7.87.

Example 20. (S)-N-[[3-[4-[5-(2-Cyanoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-

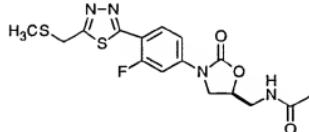
5 oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = NCCH₂CH₂). Refer to Scheme 1.



To a stirred suspension of the amide of Example 19 (110 mg) in dry THF (1.4 mL) and pyridine (0.42 mL) cooled to 0 °C is added trifluoroacetic anhydride (96 μL). The reaction mixture is stirred at 0 °C, and then at RT for 2 h. The reaction mixture is concentrated and the residue is purified by flash chromatography using 5% MeOH in CH₂Cl₂ as the eluent to afford 64 mg of the title compound.

Physical characteristics are as follows: mp 208-210 °C. ¹H-NMR (DMSO) δ 15 8.25, 7.72, 7.54, 4.77, 4.16, 3.81, 3.50, 3.48, 3.06, 1.81; % Water (KF) = 0.4; Anal. Found: C, 51.63; H, 4.18; N, 17.23; S, 7.92.

Example 21. (S)-N-[[3-[3-Fluoro-4-[5-[(methylthio)methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃SCH₂). Refer to Scheme 1.

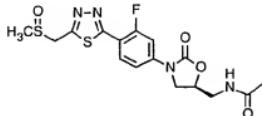


20 Step 1. (Methylthio)acetyl chloride is prepared as described in *J. Chem. Soc., Perkins Trans. I* 1996, 853.

Step 2. The thiohydrazide XVI of Example 3 (628 mg) is reacted with (methylthio)acetyl chloride (480 mg) according to the procedure of Step 5, Example 3 to afford 25 573 mg of the title compound.

Physical characteristics are as follows: mp 209-211 °C. ¹H-NMR (DMSO) δ 8.25, 7.70, 7.55, 4.76, 4.23, 4.17, 3.82, 3.42, 2.10, 1.81. Anal. Found: C, 48.36; H, 4.38; N, 14.05; S, 16.04.

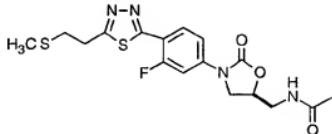
Example 22. (S)-N-[[3-[3-Fluoro-4-[5-[(methylsulfinyl)methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A. X¹ = H, X² = F, R¹ = CH₃CO, R² = CH₃S(O)CH₂). Refer to Scheme 1.



To a stirred suspension of the sulfide of Example 21 (110 mg) in 1:1 methanol/water (4.4 mL) is added sodium metaperiodate (65 mg). The reaction mixture is heated at reflux for 30 min, during which time the reaction mixture becomes homogeneous. The reaction mixture is cooled and a solid precipitate forms. The solid is removed by filtration and the filtrate is concentrated. The resulting residue is dissolved in MeOH/CH₂Cl₂, absorbed onto silica gel and purified by flash chromatography using 5% MeOH in CH₂Cl₂ as the eluent to afford 89 mg of the title compound.

Physical characteristics are as follows: mp 200-201 °C. ¹H-NMR (DMSO) δ 8.29, 8.23, 7.74, 7.55, 4.84, 4.77, 4.64, 4.18, 3.80, 3.42, 2.56, 1.81; Anal. Found: C, 46.32; H, 4.18; N, 13.38; 15.44.

Example 23. (S)-N-[[3-[3-Fluoro-4-[5-[2-(methylthio)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A. X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃SCH₂CH₂). Refer to Scheme 1.

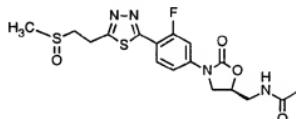


Step 1. 3-(Methylthio)propionyl chloride is prepared according to the procedure found in *Synthesis*, 1986, 1070.

Step 2. The thiohydrazide XVI of Example 3 (357 mg) is reacted with 3-(methylthio)propionyl chloride (299 mg) according to the procedure of Step 5, Example 3 to afford 404 mg of the title compound.

Physical characteristics are as follows: mp 211-213 °C. ¹H-NMR (DMSO) δ 8.24, 7.69, 7.53, 4.77, 4.17, 3.79, 3.42, 2.91, 2.10, 1.81. Anal. Found: C, 49.90; H, 4.79; N, 13.50; S, 15.37.

Example 24. (S)-N-[[3-[3-Fluoro-4-[5-[2-(methylsulfinyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = CH₃S(O)CH₂CH₂). Refer to Scheme 1.

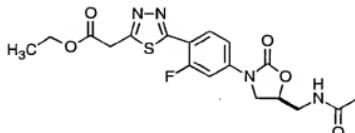


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To a stirred suspension of the sulfide of Example 23 (170 mg) in 6.4 mL MeOH/H₂O (1:1) is added sodium metaperiodate (97 mg). The reaction is heated to reflux for 15 min. during which time the reaction mixture becomes homogeneous. The 15 reaction mixture is cooled and a precipitate forms. The solid is removed by filtration and the filtrate is absorbed onto silica gel and purified by flash chromatography using 7% MeOH in CH₂Cl₂ as the eluent to afford 150 mg of the title compound as a white solid.

Physical characteristics are as follows: mp 193-914 °C. ¹H-NMR (DMSO) δ 8.24, 7.74, 7.54, 4.76, 4.17, 3.79, 3.55, 3.42, 3.16, 2.61, 1.81. Anal. Found: C, 47.70; H, 4.64; N, 13.02; S, 14.83.

Example 25. (S)-Ethyl 5-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-acetate. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃CH₂OCOCH₂). Refer to Scheme 1.

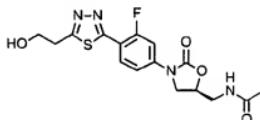


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The thiohydrazide XVI of Example 3 (587 mg) is reacted with ethyl malonyl chloride (352 mg) according to the procedure of Step 5, Example 3 to afford 539 mg of the title compound.

Physical characteristics are as follows: mp 158-159 °C. ¹H-NMR (DMSO) δ 5 8.26, 7.72, 7.52, 4.76, 4.38, 4.15, 3.79, 3.69, 3.42, 1.82, 1.21. Anal. Found: C, 50.94; H, 4.61; N, 13.22; S, 7.56.

Example 26. (S)-N-[[3-[3-Fluoro-4-[5-(2-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = HOCH₂CH₂). Refer to Scheme 1.

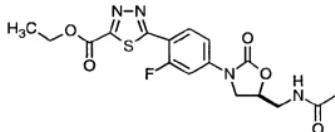


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To a stirred suspension of the ester of Example 25 (138 mg) in isopropanol (3 mL) is added a 2 M solution of lithium borohydride in THF (0.33 mL). The bright yellow reaction mixture is stirred at RT for 4 h, then quenched with water. The reaction mixture is concentrated. The residue is dissolved in MeOH/CH₂Cl₂, absorbed onto silica gel and purified by flash chromatography using 7% MeOH in CH₂Cl₂ as the eluent to afford 54.0 mg of the title compound as a white solid.

Physical characteristics are as follows: mp 192-194 °C. ¹H-NMR (DMSO) δ 8.24, 7.70, 7.51, 5.08, 4.77, 4.17, 3.76, 3.42, 3.25, 1.81. Anal. Found: C, 50.09; H, 4.62; N, 14.71; S, 8.22.

Example 27. (S)-Ethyl 5-[4-[5-(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-carboxylate. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃CH₂OCO). Refer to Scheme 1.

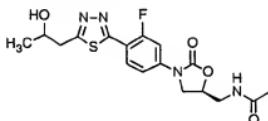


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The thiohydrazide XVI of Example 3 (364 mg) is reacted with ethyl oxalyl chloride (198 mg) according to the procedure of Step 5, Example 3 to afford 332 mg of the title compound.

Physical characteristics are as follows: mp 220-222 °C. ¹H-NMR (DMSO) δ 5 8.37, 8.23, 7.76, 7.59, 4.77, 4.43, 4.18, 3.81, 3.42, 3.29, 1.81, 1.35. Anal. Found: C, 49.53; H, 4.23; N, 13.53; S, 7.79.

Example 28. (5S)-N-[[3-[3-Fluoro-4-[5-(2-hydroxypropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = CH₃CH(OH)CH₂). Refer to Scheme 1.



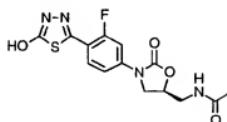
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Step 1. 3-(*tert*-Butyldimethylsiloxy)butyryl chloride is prepared according to the procedure found in *J. Org. Chem.* 1987, 52, 1780-1789.

Step 2. The thiohydrazide XVI of Example 3 (323 mg) is reacted with 3-(*tert*-butyldimethylsiloxy) butyryl chloride (468 mg) according to the procedure of Step 5, Example 3 to afford 219 mg of the title compound.

Physical characteristics are as follows: mp 200-202 °C. ¹H-NMR (CDCl₃) δ 4.35, 2.95, 1.23, 0.87, 0.07. Anal. Found: C, 51.42; H, 4.89; N, 14.03; S, 7.93.

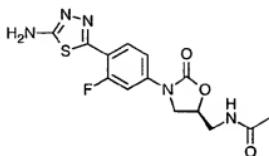
Example 29. (S)-N-[[3-[4-(4,5-Dihydro-5-oxo-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = HO). Refer to Scheme 1.



To a stirred suspension of the thiohydrazide XVI of Step 4 of Example 3 (339 mg) in THF (10 mL) is added diphosgene (0.16 mL). The reaction is heated at reflux for 1 h. The cooled reaction is concentrated. The residue is dissolved in MeOH/CH₂Cl₂, absorbed onto silica gel and purified by flash chromatography to afford 54 mg of the title compound.

Physical characteristics are as follows: mp 230-232 °C. ¹H-NMR (DMSO) δ 8.22, 7.88, 7.50, 7.46, 4.74, 4.15, 3.76, 3.41, 1.81.

Example 30. (*S*)-*N*-[[3-[4-(5-Amino-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = H₂N).

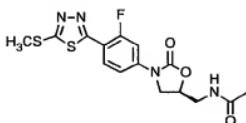


Another method of making the compounds of formula I-A is as follows: A mixture of the nitrile XII (prepared in step 1 of Example 3, 1.22 g) and thiosemicarbazide (441.2 mg) in methane sulfonic acid (5 mL) is heated at 70 °C for 45 min. The cooled reaction mixture is treated with 1 N NH₄OH, until precipitation occurs. The yellow precipitate is isolated by filtration and dried. This solid is dissolved in hot ethanol and water and the solution is made alkaline (pH 8) with 1 N NH₄OH. Upon cooling, a solid is deposited. The solid is isolated by filtration, washed with water and dried in a vacuum oven at 40 °C overnight to afford 982.7 mg of the title thiadiazole.

Physical characteristics are as follows: mp 261-262 °C (dec). ¹H NMR (DMSO) δ 8.24, 8.06, 7.62, 7.45, 4.74, 4.14, 3.76, 3.41, 1.81; % Water (KF) = 0.35%. Anal.

Found: C, 47.42; H, 4.09; N, 19.75; S, 9.14.

Example 31. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylthio)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CO, R² = CH₃S). Refer to Scheme 1.

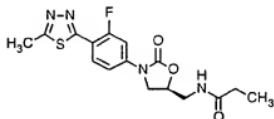


Step 1. Methyl hydrazinecarbodithioate is prepared according to the procedure in *J. Med. Chem.* 1979, 22, 855-862).

Step 2. A mixture of the nitrile XII prepared in Step 1, Example 3 (266 mg) and methyl hydrazinecarbodithioate (293 mg) in methane sulfonic acid (4 mL) is heated at 65 °C for 18 h. The cooled reaction mixture is cooled and treated with 1 M aqueous NH₄OH after which a solid precipitate forms. The solid is isolated by filtration. The solid is dissolved in MeOH/CH₂Cl₂, absorbed onto silica gel and purified using a Biotage 40 S column using 3% MeOH in CH₂Cl₂ as eluent to afford 124.5 mg of the title compound as a white solid.

5 Physical characteristics are as follows: mp 196-198 °C. ¹H-NMR (DMSO) δ 8.23, 7.75, 7.54, 4.77, 4.16, 3.78, 3.42, 2.80, 1.81. % Water (KF) 2.50; Anal. Found: C, 10 45.51; H, 3.88; N, 14.15; S, 16.22.

Example 32. (S)-N-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide. (I-A, X¹ = H, X² = F, R¹ = CH₃CH₂CO, R² = CH₃). Refer to Scheme 1.

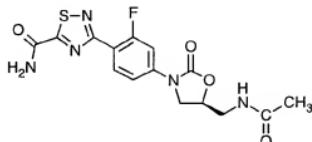


15 Step 1. To a solution of hydroxylamine hydrochloride (732 mg) in pyridine (25 mL) is added the title compound of Example 3 (693 mg). The mixture turns homogenous with the addition of EtOH (2.5 mL). The reaction mixture is heated to reflux for 4 hours. The reaction is cooled to room temperature and the precipitated product is collected by filtration to afford 124 mg of the aminomethyl oxazolidinone.

20 Step 2. To a suspension of the compound prepared in Step 1 (200 mg) in 10 mL of CH₂Cl₂ is added propionyl chloride (113 μL) and triethylamine (362 μL). The reaction is heated to 70 °C for 2 hours. The reaction is concentrated and the residue is triturated with Et₂O. Further purification by chromatography using 5% MeOH/CH₂Cl₂ as eluent gives 189 mg of the title compound.

25 Physical characteristics are as follows: mp 249-251 °C. ¹H-NMR (DMSO) δ 8.20, 7.69, 7.51, 4.78, 4.17, 3.82, 3.43, 2.77, 2.08, 0.93. Anal. Found: C, 52.78; H, 4.66; N, 15.32.

Example 33. (*S*)-3-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,2,4-thiadiazole-5-carboxamide (I-B, $X^1 = H$, $X^2 = F$, $R^1 = COCH_3$, $R^2 = NH_2CO$). Refer to Scheme 2.



5 Step 1. The nitrile XII (prepared in step 1 of Example 3, 1.11g) is dissolved in warm DMSO (3.0 mL) and powdered potassium carbonate (100 mg) is added. The mixture is cooled to 15 °C and 30% hydrogen peroxide (900 uL) is added. A vigorous exothermic reaction begins and after it subsides, the cooling bath is removed and the reaction stirred 15 minutes at 20 °C. The reaction is diluted with ethanol (100 mL) and 10 toluene (200 mL) and filtered, then concentrated *in vacuo* to an orange oil. The oil is chromatographed over silica gel, eluting with 10% methanol in methylene chloride. The product is recrystallized from ethyl acetate to give 840 mg of the product XVII as white crystals.

15 Physical characteristics as follows: mp 219-20 °C; 1H NMR (300 MHz, DMSO) δ 8.27, 7.71, 7.56, 7.53, 7.34, 4.72, 4.12, 3.74, 3.40, 1.80; Anal. Found: C, 52.55; H, 4.90; N, 14.12.

20 Step 2. The amide XVII prepared in step 1 (100mg) is dispersed in acetonitrile (4 mL) and chlorocarbonyl sulphenyl chloride (70 uL) is added. The reaction is warmed to 80 °C for 1.5 hours. The solvent is evaporated and the residue is chromatographed over silica gel, eluting with 5% methanol in methylene chloride to give the product XVIII (47 mg) as a tan solid.

Physical characteristics are as follows: mp 175 °C, dec. 1H NMR (300 MHz, DMSO) δ 8.24, 7.92, 7.65, 7.51, 4.75, 4.16, 3.78, 3.41, 1.81;

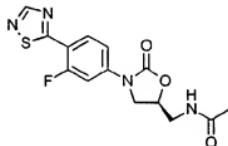
25 Step 3. The 1,3,4-oxathiazole-2-one XVIII prepared in step 2 (40 mg) is mixed with ethylcyanoformate (1.5 mL) in toluene (3.0 mL) and heated to reflux (130 °C) for 17 hours. The solvent is evaporated under a stream of dry nitrogen and the residue is chromatographed over silica gel, eluting with 5 % methanol in methylene chloride to afford 21 mg of the ethyl thiadiazolecarboxylate (I-B, $R^2 = CH_3CH_2CO$) as a yellow solid.

Physical characteristics are as follows: mp 115-117 °C, ¹HNMR (300 MHz, CDCl₃) δ 8.25, 7.60, 7.28, 6.43, 4.83, 4.53, 4.11, 3.84, 3.69, 2.03, 1.46.

Step 4. The ethyl thiadiazolecarboxylate prepared in Step 3 (175 mg) is dissolved in methanol (10 mL) and methanol saturated with ammonia (5 mL) is added. The reaction is stirred at 20°C for 2 hours. A tan precipitate forms. The solution is diluted with warm methanol (10 mL) and treated with decolorizing carbon and filtered. The solution is concentrated and the residue is recrystallized from ethyl acetate/ methanol, to give 120 mg of the title compound as tan crystals.

Physical characteristics are as follows: mp = 238-240°C. ¹H NMR (300 MHz, DMSO) δ 8.53, 8.26, 8.24, 7.67, 7.49, 4.77, 4.18, 3.80, 3.42, 1.82. HRMS (FAB) found for C₁₅H₁₄FN₅O₄S+H₁, 380.0822.

Example 34. (S)-N-[[3-[3-Fluoro-4-(1,2,4-thiadiazol-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-C, X¹ = F, X² = H, R¹ = COCH₃, R² = H). Refer to Scheme 3.



15

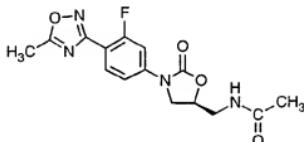
Step 1: A mixture of thioamide XIII, prepared as described in Step 2 of Example 3 (0.500 g) and N,N-dimethylformamide dimethyl acetal (257 μL) in dry methylene chloride (3.2 mL) is stirred under nitrogen for 1 hr. The reaction mixture is then triturated with diethyl ether and the orange precipitate filtered and dried under reduced pressure to give the amidine which is not further purified but is used directly in the next step. mp 163 - 165 °C (decomp.).

Step 2: A mixture of the amidine prepared in step 1 (0.250 g) in absolute ethanol (1.7 mL) and pyridine (0.11 mL) under nitrogen is treated with a solution of hydroxylamine-O-sulfonic acid (85 mg) in methanol (1.0 mL). The resulting mixture is stirred at ambient temperature for 45 mins, concentrated under reduced pressure, rediluted with water (25 mL) and extracted with methanol/chloroform (10/90, 4 x 50 mL). The combined organic phases are then washed with aqueous sodium hydroxide (0.1 M, 50 mL), water (50 mL) and saline (20 mL), dried over anhydrous sodium sulfate and concentrated under reduced pressure to give the crude product. Purification by reverse

phase HPLC (Zorbax SB-18 column, 20 - 60% acetonitrile/water eluent) gives 21 mg of the title compound.

Physical characteristics are as follows: mp 199-200°C. ^1H NMR (CDCl_3) δ 8.71, 8.34, 7.76, 7.32, 6.17, 4.85, 4.13, 3.86, 3.72, 2.05.

5 Example 35. (*S*)-*N*-[(3-[3-Fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-oxo-5-oxazolidinyl)methyl]acetamide (I - H where X^1 is H , X^2 is F , R^1 is COCH_3 and R^2 is CH_3). Refer to Scheme 8.



Step 1. The nitrile XII (prepared in step 1 of Example 3, 2.77g), hydroxylamine hydrochloride (2.08g) and powdered sodium carbonate (4.23g) are dissolved in methanol (30 mL). The reaction is warmed to reflux for 2.5 hours and turns very dark in color. The reaction is diluted with 1:1 methylene chloride and methanol (50 mL) and filtered through celite. The celite is washed with another aliquot of solvent (50 mL) and the combined filtrates are concentrated in vacuo. The residue is chromatographed over silica gel, eluting with 10% methanol in methylene chloride to give a yellow foam which is crystallized from methanol/ethyl acetate to give 2.2 g of the hydroxyamide XXII as a yellow crystalline solid.

10

15

Physical characteristics are as follows: mp 196-7 °C dec.; ^1H NMR (300 MHz, DMSO) δ 9.63, 8.26, 7.50, 7.31, 5.78, 4.75, 4.13, 3.75, 3.42, 1.83; Anal. Found: C, 50.23; H, 4.89; N, 17.96.

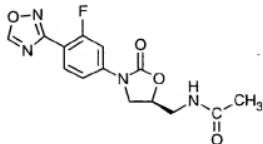
20

Step 2. The hydroxyamide XXII prepared in step 1 (310 mg) is dissolved in acetic anhydride (3 mL) and heated at 120 °C for 3 hours. The solvent is evaporated under a stream of dry nitrogen and the residue is chromatographed over silica gel, eluting with 10 % methanol in methylene chloride to give a white solid. The product is recrystallized from ethyl acetate / hexane as white needles to afford 145 mg of title product.

25

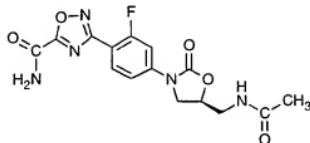
Physical characteristics are as follows: mp 177-9 °C. ^1H NMR (300 MHz, CDCl_3) δ 8.02, 7.62, 7.31, 6.13, 4.82, 4.10, 3.83, 3.68, 2.66, 2.03; Anal. Found: C, 53.55; H, 4.64; N, 16.41.

Example 36. (*S*)-*N*-[[3-[3-Fluoro-4-(1,2,4-oxadiazol-3-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-H where X¹ is H, X² is F, R¹ is COCH₃, and R² is H). Refer to Scheme 8.



5 The hydroxyamidine XXII (prepared in step 1 of Example 35, 200 mg) is dispersed in triethyl orthoformate (3 mL) and heated at reflux until all starting material is gone by TLC. Triethylamine (3 equivalents) and methanol (2 mL) are added and the mixture is stirred at 50 °C for 17 hours. The solvent is evaporated and the residue is chromatographed over silica gel to give 47 mg of the desired product as a white solid.
10 Physical characteristics are as follows: mp 197-9 °C. ¹H NMR (300 MHz, DMSO) δ 9.77, 8.27, 8.08, 7.75, 7.56, 4.78, 4.19, 3.81, 3.44, 1.83; Anal. Found: C, 52.51; H, 4.45; N, 16.37.

Example 37. (*S*)-3-[4-[5-[(Acetylaminomethyl)-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,2,4-oxadiazole-5-carboxamide (I-H where X¹ is H, X² is F, R¹ is COCH₃, and R² is H₂NCO). Refer to Scheme 8.
15



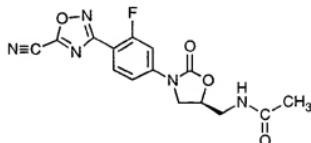
Step 1. The hydroxyamidine XXII (prepared in step 1 of example 35, 930 mg), is dissolved in pyridine (1.0 mL) and methylene chloride (10mL) and the solution is stirred at 20 °C. Ethyl oxalyl chloride (285 uL) is added dropwise and the reaction is stirred for 20 1 hour. The solvent is evaporated under a stream of nitrogen and the residue is chromatographed over silica gel, eluting with 10% methanol in methylene chloride, to give 700 mg of crude oxadiazole ester.

Step 2. The crude ester prepared in step 1 (700 mg) is dissolved in methanol (15 mL) and methanol saturated with ammonia (10 mL) is added. The reaction is stirred 3 hours at ambient temperature and then cooled in a refrigerator for 2 hours. The product

crystallizes from the reaction mixture and is collected by filtration to afford 315 mg of title product.

Physical characteristics are as follows: mp 218-20 °C; ¹H NMR (300 MHz, DMSO) δ 8.80, 8.48, 8.27, 8.08, 7.74, 7.58, 4.80, 4.20, 3.82, 3.45, 1.84; Anal. 5 Found: C, 48.35; H, 4.13; N, 18.48.

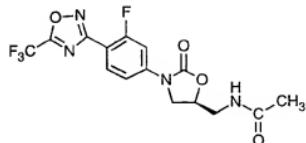
Example 38. (*S*)-*N*-[[3-[4-(5-Cyano-1,2,4-oxadiazol-3-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I -H where X¹ is H, X² is F, R¹ is COCH₃ and R² is CN).



10 The title amide of Example 37 (150 mg) is dissolved in pyridine (1.0 mL) and THF (2.0 mL) and cooled to 0 °C. Trifluoroacetic anhydride (170 uL) is added. The reaction is stirred for 20 minutes, then allowed to warm to ambient temperature and stirred for 17 hours. The solvent is evaporated under dry nitrogen and the residue is chromatographed over silica gel, eluting with 10% methanol in methylene chloride to 15 give a white solid. Recrystallization from ethyl acetate/hexane gives 110 mg of the title product as white needles.

Physical characteristics are as follows: mp 200-2 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.98, 7.67, 7.31, 7.26, 4.78, 4.04, 3.83, 3.58, 1.93; Anal. Found: C, 51.98; H, 3.72; N, 20.00.

20 Example 39. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I -H where X¹ is H, X² is F, R¹ is COCH₃ and R² is CF₃). Refer to Scheme 8.

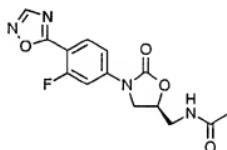


The hydroxyamidine XXII prepared in step 1 of Example 35 (310 mg) is 25 dissolved in pyridine (3.0 mL) and trifluoroacetic anhydride (282 uL) is added at 20 °C.

The reaction is stirred for 10 minutes, and then warmed to reflux for 30 minutes. The reaction is allowed to slowly cool and then the solvent is evaporated under a stream of dry nitrogen. The residue is chromatographed over silica gel, eluting with 10% methanol in methylene chloride to give a white solid which is recrystallized from ethyl acetate/hexane to afford 295 mg of the title product.

Physical characteristics are as follows: mp 192-3 °C. ^1H NMR (300 MHz, DMSO) δ 8.27, 8.10, 7.74, 7.60, 4.80, 4.20, 3.81, 3.44, 1.83. Anal. Found: C, 46.21; H, 3.25; N, 14.29.

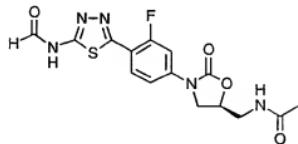
Example 40. (*S*)-*N*-[[3-[3-Fluoro-4-(1,2,4-oxadiazol-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-I, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{COCH}_3$, $\text{R}^2 = \text{H}$).



The title compound (57 mg) is obtained as a byproduct from the procedure of example 34.

Physical characteristics are as follows: mp 199-200°C. ^1H NMR (CDCl_3) δ 9.12, 8.24, 8.17, 7.73, 7.59, 4.79, 4.20, 3.82, 3.44, 1.83. Anal. Found: C, 52.16; H, 4.13; N, 17.34.

Example 41. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(formylamino)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-A, $\text{X}^1 = \text{H}$, $\text{X}^2 = \text{F}$, $\text{R}^1 = \text{COCH}_3$, $\text{R}^2 = \text{HC(O)NH}$).



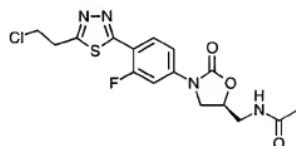
To a stirred suspension of the compound of Example 30 (184 mg) in dry THF (5 mL) is added 1H-benzotriazole-1-carboxaldehyde (168 mg). The reaction mixture is heated at reflux for 48 hours, cooled and concentrated. The residue is dissolved in

EtOH/CH₃CN, absorbed onto silica gel and purified by flash chromatography using 7% MeOH in CH₂Cl₂ as the eluent to yield 155 mg of the title compound as a white solid.

Physical characteristics are as follows: mp 259-260 °C (dec). ¹H NMR (DMSO-*d*₆) δ 12.9, 8.53, 8.25, 7.71, 7.53, 4.76, 4.17, 3.79, 3.42, 1.81. % Water (KF) = 3.65.

5 Anal. Found: C, 46.29; H, 3.92; N, 17.65; S, 8.04.

Example 42. (*S*)-*N*-[[3-[4-[5-(2-Chloroethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (I-A, X¹ = F, X² = H, R¹ = COCH₃, R² = ClCH₂CH₂).



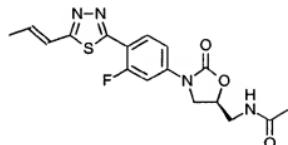
10

The thiohydrazide XVI of Example 3 (250 mg) is reacted with acryloyl chloride (125 μL) according to the procedure of Step 5, Example 3 to afford 196 mg of the title compound.

Physical characteristics are as follows: mp 178-180 °C. ¹H NMR (DMSO-*d*₆) δ

15 8.26, 7.73, 7.53, 4.76, 4.18, 4.05, 3.80, 3.63, 3.43, 1.82. Anal. Found: C, 48.94; H, 4.08; N, 13.96.

Example 43. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(1-propenyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = COCH₃, R² = CH₃CH=CH).

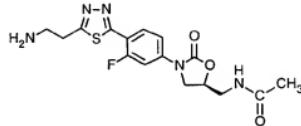


20

The thiohydrazide XVI from Step 4 of Example 3 (200 mg) is reacted with 3-butenoyl chloride (127 mg) according to the procedure of Step 5, Example 3 to afford 120 mg of the title compound.

Physical characteristics are as follows: mp 242-244 °C. ^1H NMR (DMSO- d_6) δ 8.27, 7.71, 7.53, 6.88, 6.76, 4.77, 3.80, 3.42, 1.94, 1.82. HRMS (EI) Found for $\text{C}_{17}\text{H}_{17}\text{FN}_4\text{O}_3\text{S}$, 377.1075.

Example 44. (*S*)-*N*-[[3-[4-[5-(2-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{H}_2\text{NCH}_2\text{CH}_2$). Refer to Scheme I.



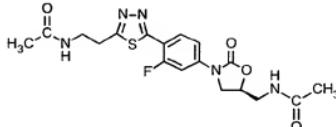
Step 1. Fmoc- β -Ala-OH (1.0 g) is suspended in methylene chloride at room temperature under nitrogen. Oxalyl chloride (298 μL) is added followed by two drops of DMF. After stirring overnight at room temperature, the reaction is concentrated to afford 0.75 g of the acid chloride (Fmoc- β -Ala-Cl).

Step 2. The thiohydrazide XVI of Example 3 (210 mg) is reacted with Fmoc- β -Ala-Cl (275 mg, from Step 1) according to the procedure of Step 5, Example 3 to afford 358 mg of the Fmoc-protected title compound.

Step 3. The Fmoc-protected amine prepared in Step 2 (1.3 g) is dissolved in piperidine (30 mL) and stirred for 1 hour at room temperature. The reaction is concentrated and the residue is purified by flash chromatography using 5% MeOH (saturated with NH_3) in CH_2Cl_2 to afford 0.59 g of the title compound.

Physical characteristics are as follows: mp 195-197 °C. ^1H NMR (DMSO- d_6) δ 8.22, 7.70, 7.52, 4.76, 4.17, 3.80, 3.42, 3.32, 3.15, 2.91, 1.82. Anal. Found: C, 50.19; H, 5.07; N, 17.92; S, 8.02.

Example 45. (*S*)-*N*-[[3-[4-[5-[2-(Acetylamino)ethyl]-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{CH}_3\text{C}(\text{O})\text{NHCH}_2\text{CH}_2$). Refer to Scheme I.



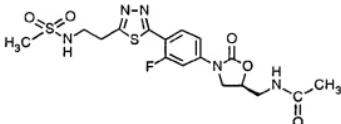
25

The thiadiazole prepared in Example 44, Step 3 (300 mg) is combined with acetic anhydride (97 μ L) and pyridine (199 μ L) in 20 mL of CH_2Cl_2 . The reaction is heated overnight and then concentrated in vacuo. The residue is dissolved in CH_2Cl_2 and

5 MeOH, absorbed onto silica, and purified by flash chromatography using 5% MeOH in CH_2Cl_2 as eluent to afford 251 mg of the title compound.

Physical characteristics are as follows: mp 259-261 $^{\circ}$ C. ^1H NMR (DMSO- d_6) δ 8.25, 8.08, 7.70, 7.53, 4.77, 4.17, 3.79, 3.42, 3.26, 1.82, 1.78. Anal. Found: C, 51.25; H, 4.83; N, 16.59; S, 7.46.

10 Example 46. (S)-*N*-[[3-[3-Fluoro-4-[5-[2-[(methylsulfonyl)amino]ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{CH}_3\text{SO}_2\text{NHCH}_2\text{CH}_2$). Refer to Scheme I.

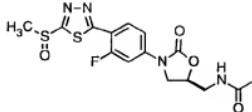


The thiadiazole prepared in Example 44, Step 3 (300 mg) is suspended in CH_2Cl_2 (10 mL) and methanesulfonyl chloride (127 μ L) and triethylamine (458 μ L) are added.

15 The reaction is heated to 60 $^{\circ}$ C for 3 hours and then concentrated to dryness. The residue is taken up in CH_2Cl_2 and MeOH, absorbed onto silica gel, and purified by flash chromatography using 5% MeOH in CHCl_3 as eluent to afford 145 mg of the title compound.

20 Physical characteristics are as follows: mp 213-214. ^1H NMR (DMSO- d_6) δ 8.25, 7.71, 7.53, 7.30, 4.77, 4.17, 3.81, 3.35, 2.92, 1.82. Anal. Found: C, 44.19; H, 4.57; N, 15.08; S, 13.57.

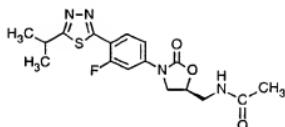
Example 47. (5S)-*N*-[[3-[3-Fluoro-4-[5-(methylsulfinyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $25 \text{R}^2 = \text{CH}_3\text{SO}$). Refer to Scheme I.



The sulfide prepared in Step 2 of Example 31 (252 mg) is suspended in CH₃OH (5 mL) and water (5 mL). Sodium metaperiodate (155 mg) is added with stirring. The reaction mixture is heated at reflux for 18 hours and then cooled and concentrated. The residue is dissolved in CH₃OH and CH₂Cl₂, absorbed onto silica gel and purified by flash chromatography using 20% CH₃CN in ethyl acetate to 5% CH₃OH in CH₂Cl₂ as the eluent to afford 104 mg of the title compound.

Physical characteristics are as follows: mp 213-215 °C. ¹H NMR (DMSO-*d*₆) δ 8.31, 7.76, 7.59, 4.77, 4.18, 3.81, 3.42, 3.17, 1.81. Anal. Found: C, 44.87; H, 3.72; N, 10 13.88; S, 15.61.

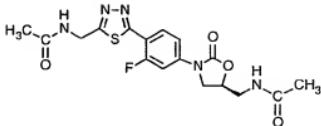
Example 48. (S)-*N*-[[3-[3-Fluoro-4-[5-(1-methylethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = (CH₃)₂CH). Refer to Scheme I.



15 The thiohydrazide XVI prepared in Example 3, Step 4 (300 mg) is reacted with isobutyryl chloride (125 μL) according to the procedure of Step 5, Example 3 to afford 150 mg of the title compound.

Physical characteristics are as follows: mp 158 °C. ¹H NMR (DMSO-*d*₆) δ 8.22, 7.70, 7.52, 4.73, 3.79, 3.79, 3.50, 3.42, 1.82, 1.39. Anal. Found: C, 53.63; H, 5.18; N, 20 14.81; S, 8.43.

Example 49. (S)-*N*-[[5-[4-[Acetylaminomethyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃C(O)NHCH₃). Refer to Scheme I.

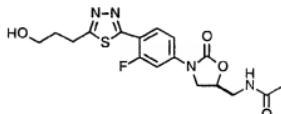


25 The amine of Example 6, Step 2 (300 mg) is mixed with CH₂Cl₂ (10 mL) and triethylamine (457 μL). The temperature is lowered to 0 °C and acetyl chloride (117 μL)

is added. The reaction is warmed to RT and then concentrated in vacuo. The solid is dissolved in CH_2Cl_2 and MeOH, absorbed onto silica gel, and flash chromatographed using 6% MeOH in CH_2Cl_2 as eluent to give 301 mg of the title compound.

Physical characteristics are as follows: mp 233-235 °C. ^1H NMR (DMSO- d_6) δ 5 8.90, 8.25, 7.70, 7.51, 4.77, 4.65, 4.17, 3.81, 3.41, 1.89, 1.82. Anal. Found: C, 49.98; H, 4.45; N, 16.95.

Example 50. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-hydroxypropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A. $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{HOCH}_2\text{CH}_2\text{CH}_2$). Refer to Scheme I.



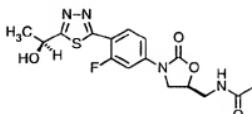
10

Step 1. 4-[(*tert*-Butyldiphenylsilyl)oxy]butyryl chloride is prepared as described in *J. Org. Chem.*, 1996, 61, 2413-2427.

Step 2. The thiohydrazide XVI prepared in Example 3, Step 4 (352 mg) is reacted 15 with the acid chloride prepared in Step 1 of this example (776 mg) according to the procedure of Example 3, Step 5. The residue is treated with methanol to afford 363 mg of the title compound.

Physical characteristics are as follows: mp 195-197 °C. ^1H NMR (DMSO- d_6) δ 8.23, 7.70, 7.51, 4.76, 4.62, 4.16, 3.79, 3.42, 3.16, 1.89, 1.81; Anal. Found: C, 51.33; H, 20 4.97; N, 14.06; S, 7.42.

Example 51. [*S*-(*R*^{*}-*R*^{*})-*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A. $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{R}^2 = \text{S}-\text{CH}_2\text{CH}(\text{OH})$). Refer to Scheme I.



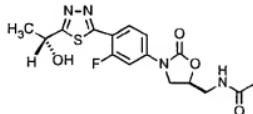
25 Step 1. The *t*-butyldimethylsilyl ether of L-lactic acid chloride is prepared as described in *Tetrahedron Letters*, 1996, 37, 3515-3518.

Step 2. The thiohydrazide XVI prepared in Example 3, Step 4 (414 mg) is reacted with the acid chloride prepared in Step 1 of this example (563 mg) according to the procedure of Example 3, Step 5. The residue is treated with methanol to afford 383 mg of the title compound.

5 Physical characteristics are as follows: mp 202-203 °C. ^1H NMR (DMSO- d_6) δ 8.25, 7.70, 7.52, 6.39, 5.15, 4.76, 4.17, 3.79, 3.42, 1.81, 1.53. Anal. Found: C, 50.28; H, 4.44; N, 14.73; S, 8.42.

Example 52. $(S\text{-}(R^*,S^*))\text{-N-}[[3\text{-}[3\text{-Fluoro-4\text{-[5\text{-}(1\text{-hydroxyethyl)\text{-}1,3,4-thiadiazol-2\text{-yl]\text{-}phenyl]\text{-}2\text{-oxo-5\text{-oxazolidinyl]\text{-}methyl]\text{-}acetamide. (I\text{-}A, X}^1\text{ = F, X}^2\text{ = H, R}^1\text{ = CH}_3\text{CO, R}^2\text{ = R\text{-}CH}_3\text{CH(OH))}. Refer to Scheme I.$

10



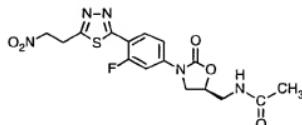
Step 1. The *t*-butyldimethylsilyl ether of R-lactic acid chloride is prepared as described in *Tetrahedron Letters*, 1996, 37, 3515-3518.

15 Step 2. The thiohydrazide XVI of Example 3, Step 4 (414 mg) is reacted with the acid chloride prepared in Step 1 of this example (563 mg) according to the procedure of Example 3, Step 5. The residue is treated with methanol to afford 383 mg of the title compound.

Physical characteristics are as follows: mp 209-210 °C; ^1H NMR (DMSO- d_6) δ 20 8.23, 7.70, 7.51, 6.41, 5.15, 4.76, 4.17, 3.79, 3.42, 1.81, 1.50; Anal. Found: C, 50.32; H, 4.66; N, 14.56; S, 8.27.

Example 53. $(S)\text{-N-}[[3\text{-[3\text{-Fluoro-4\text{-[5\text{-}(2\text{-nitroethyl)\text{-}1,3,4-thiadiazol-2\text{-yl]\text{-}phenyl]\text{-}2\text{-oxo-5\text{-oxazolidinyl]\text{-}methyl]\text{-}acetamide. (I\text{-}A, X}^1\text{ = F, X}^2\text{ = H, R}^1\text{ = CH}_3\text{CO, R}^2\text{ = O}_2\text{NCH}_2\text{CH}_2\text{). Refer to Scheme I.}$

25

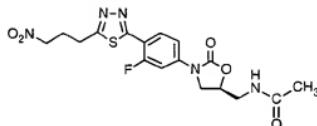


Step 1. 3-Nitropropionyl chloride is prepared according to the procedure of *J. Pharm. Sci.* 1978, 67, 421-3.

Step 2. The thiohydrazide XVI of Example 3, Step 4 (300 mg) is reacted with the acid chloride prepared in Step 1 of this example (164 mg) according to the procedure of Example 3, Step 5.

Physical characteristics are as follows: mp 195-197 °C. ^1H NMR (DMSO- d_6) δ 8.23, 7.71, 7.53, 5.09, 4.76, 4.17, 3.81, 3.42, 1.82. Anal. Found: C, 46.87; H, 4.19; N, 16.79; S, 7.70.

Example 54. (S)-*N*-[[3-[3-Fluoro-4-[5-(3-nitropropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X^1 = F, X^2 = H, R^1 = CH_3CO , R^2 = $\text{O}_2\text{NCH}_2\text{CH}_2\text{CH}_2$). Refer to Scheme I.

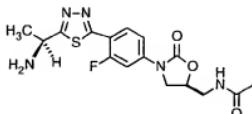


Step 1. 4-Nitrobutyryl chloride is prepared according to the procedure of *Chem. Pharm. Bull.* 1992, 40, 2338-2343.

Step 2. The thiohydrazide XVI of Example 3, step 4 (1.44 g) is reacted with the acid chloride prepared in Step 1 of this example (868 mg) according to the procedure of Example 3, Step 5.

Physical characteristics are as follows: mp 183-185 °C. ^1H NMR (DMSO- d_6) δ 8.26, 7.71, 7.53, 4.76, 4.69, 4.17, 3.80, 3.42, 3.24, 2.40, 1.82. Anal. Found: C, 48.50; H, 4.44; N, 16.10; S, 7.45.

Example 55. [S-(R*,R*)]-*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X^1 = F, X^2 = H, R^1 = CH_3CO , R^2 = $S\text{-CH}_2\text{CHNH}_2$). Refer to Scheme I.

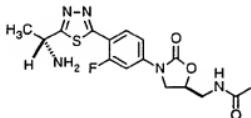


Step 1. The thiohydrazide XVI of Example 3, Step 4 (383 mg) is reacted with FMOC-Ala-Cl (503 mg) according to the procedure of Example 3, Step 5 to afford a protected aminoethyl thiadiazole.

Step 2. The protected thiadiazole prepared in step 1 (355 mg) is stirred in 5 piperidine (8.4 mL) at room temperature for 1 hour and then concentrated. The residue is triturated with ether and the solid is isolated by filtration and dried. The solid is dissolved in methanol/CH₂Cl₂, absorbed onto silica gel and purified by flash chromatography using 7% methanol in CH₂Cl₂ as the eluent to afford 211 mg of the title compound.

10 Physical characteristics are as follows: mp 184-186 °C. ¹H NMR (DMSO-*d*₆) δ 8.24, 7.70, 7.50, 4.76, 4.40, 4.17, 3.78, 3.42, 2.57, 1.81, 1.44. Anal. Found: C, 49.49; H, 5.10; N, 17.93; S, 8.11.

Example 56. [S-(*R*^{*,S}₂)-N-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = 15 H, R¹ = CH₃CO, R² = *R*-CH₂CHNH₂). Refer to Scheme I.

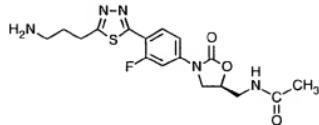


Step 1. The thiohydrazide XVI of Example 3, Step 4 (359 mg) is reacted with FMOC-D-Ala-Cl (472 μL) according to the procedure of Example 3, Step 5 to afford a protected aminoethyl thiadiazole.

20 Step 2. A suspension of the thiadiazole prepared in Step 1 of this example (390 mg) in piperidine (9 mL) is stirred at room temperature for 1 hour and then concentrated. The residue is triturated with ether and the solid is isolated by filtration and dried. The solid is dissolved in methanol/CH₂Cl₂, absorbed onto silica gel and purified by flash chromatography using 7% methanol in CH₂Cl₂ as the eluent to afford 229 mg of the title compound.

25 Physical characteristics are as follows: mp 201-203 °C. ¹H NMR (DMSO-*d*₆) δ 8.24, 7.70, 7.51, 4.76, 4.40, 4.16, 3.79, 3.42, 3.33, 2.63, 1.81, 1.44. Anal. Found: C, 49.27; H, 5.03; N, 17.90; S, 8.07.

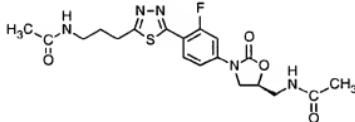
Example 57. (*S*)-*N*-[[3-[4-[5-(3-Aminopropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = \text{CH}_3\text{CO}$, $R^2 = \text{H}_2\text{NCH}_2\text{CH}_2\text{CH}_2$). Refer to Scheme I.



5 The 3-nitropropylthiadiazole prepared in Example 54, Step 2 (400 mg) is dissolved in MeOH (100 mL) and DMF (25 mL). Raney Nickel (approx. 1.0 g) is added and the reaction is placed on a Parr apparatus under H_2 (45 psi) overnight. The reaction is filtered and concentrated. The residue is taken up in CHCl_3 and MeOH, absorbed onto silica gel, and purified by flash chromatography using 1.5% MeOH (saturated with NH_3) in CH_2Cl_2 as eluent to afford 193 mg of the title compound.

10 Physical characteristics are as follows: mp 181-183 °C. ^1H NMR (DMSO- d_6) δ 8.23, 7.70, 7.52, 4.77, 4.16, 3.81, 3.42, 3.17, 2.61, 1.82. Anal. Found: C, 51.36; H, 5.04; N, 17.23; S, 7.85.

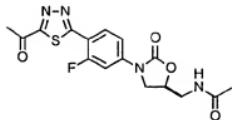
15 Example 58. (*S*)-*N*-[3-[5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]propyl]acetamide. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = \text{CH}_3\text{CO}$, $R^2 = \text{CH}_3\text{C}(\text{O})\text{NHCH}_2\text{CH}_2\text{CH}_2$). Refer to Scheme I.



20 The 3-aminopropylthiadiazole prepared in Example 57 (300 mg) is dissolved in CH_2Cl_2 (20 mL) at room temperature under nitrogen. Acetic anhydride (90 μL) and pyridine (185 μL) are added, and the reaction is heated to reflux for 1 hour. The reaction is then cooled and concentrated. The residue is dissolved in MeOH and CH_2Cl_2 , absorbed onto silica gel, and purified by flash chromatography using 3% MeOH (saturated with NH_3) in CH_2Cl_2 as eluent to give 287 mg of the title compound.

Physical characteristics follow: mp 229-230 °C. ^1H NMR (DMSO- d_6) δ 8.23, 7.93, 7.71, 7.53, 4.77, 4.17, 3.82, 3.42, 3.13, 1.88, 1.82, 1.79. Anal. Found: C, 52.04; H, 5.10; N, 15.89; S, 7.27.

Example 59. (S)-*N*-[[3-[4-(5-Acetyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X^1 = F, X^2 = H, R^1 = CH_3CO , R^2 = CH_3CO). Refer to Scheme I.

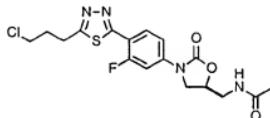


Step 1. Pyruvyl chloride is prepared as described in *Synthesis*. 1975, 163-164.

Step 2. The thiohydrazide XVI of Example 3, Step 4 (959 mg) is reacted with the acid chloride prepared in Step 1 of this example (655 mg) according to the procedure of Example 3, Step 5 to give 442 mg of the title compound.

Physical characteristics are as follows: mp 242-244 °C. ^1H NMR (DMSO- d_6) δ 8.35, 8.27, 7.75, 7.56, 4.78, 4.18, 3.81, 3.43, 2.74, 1.81. Anal. Found: C, 50.43; H, 4.03; N, 14.75; S, 8.35.

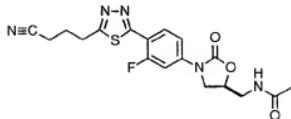
Example 60. (S)-*N*-[[3-[4-[5-(3-Chloropropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X^1 = F, X^2 = H, R^1 = CH_3CO , R^2 = $\text{ClCH}_2\text{CH}_2\text{CH}_2$). Refer to Scheme I.



The thiohydrazide XVI of Example 3, Step 4 (322 mg) is reacted with 4-chlorobutryl chloride (140 μL) according to the procedure of Example 3, Step 5 to give the title compound (306 mg).

Physical characteristics are as follows: mp 199-200 °C. ^1H NMR (DMSO- d_6) δ 8.23, 7.73, 7.52, 4.77, 4.17, 3.79, 3.74, 3.42, 3.29, 2.27, 1.8. Anal. Found: C, 49.08; H, 4.50; N, 13.45; Cl, 8.52; S, 7.62.

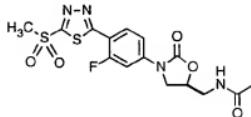
Example 61. (*S*)-*N*-[[3-[4-[5-(3-Cyanopropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = NCCH₂CH₂CH₃). Refer to Scheme I.



5 A mixture of the chloride prepared in Example 60 (145 mg) and tetrabutylammonium cyanide (189 mg) in dry DMF (3.5 mL) is heated at 80 °C for 30 minutes. The DMF is removed under vacuum and the residue is dissolved in methanol/CH₂Cl₂. The solid that forms is isolated by filtration and dried to afford 81 mg of the title compound.

10 Physical characteristics are as follows: mp 186-187 °C. ¹H NMR (DMSO-*d*₆) δ 8.24, 7.73, 7.55, 4.77, 4.17, 3.79, 3.42, 3.24, 2.63, 2.08, 1.81. Anal. Found: C, 51.05; H, 4.74; N, 16.47; S, 7.59.

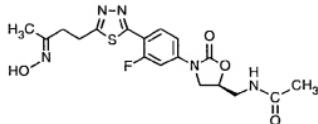
Example 62. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylsulfonyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃SO₂). Refer to Scheme I.



20 The sulfide prepared in Example 31, Step 2 (206 mg) is dissolved in methanol (2 mL) and water (2 mL). Oxone (431 mg) is added and the reaction mixture is heated at reflux for 4 hours. The reaction mixture is cooled and the solid is separated by filtration and then washed with water. The solid is dissolved in methanol/CH₂Cl₂, absorbed onto 25 silica gel and purified by flash chromatography using 6% methanol in CH₂Cl₂ as the eluent to afford 166 mg of the title compound.

Physical characteristics are as follows: mp 244-245 °C. ¹H NMR (DMSO-*d*₆) δ 8.36, 8.24, 7.80, 7.62, 4.78, 4.19, 3.81, 3.65, 3.43, 1.81. Anal. Found: C, 43.08; H, 3.90; N, 13.28; S, 14.92.

Example 63. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[3-(hydroxyimino)butyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = \text{CH}_3\text{CO}$, $R^2 = \text{CH}_3\text{C}(\text{NOH})\text{CH}_2\text{CH}_2$). Refer to Scheme I.

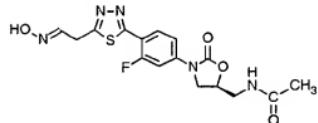


5 The ketone prepared in Example 16, Step 2 (330 mg) is dissolved in EtOH (20 mL) and CH_2Cl_2 (15 mL). Hydroxylamine hydrochloride (169 mg) is added and the reaction is heated to 60 °C overnight under a nitrogen atmosphere. The reaction is then concentrated and the residue is dissolved in MeOH and CH_2Cl_2 , absorbed onto silica, and purified by flash chromatography using 3% MeOH in CH_2Cl_2 as eluent to afford 304 mg
10 of the title compound.

Physical characteristics are as follows: mp 218-220 °C. ^1H NMR (DMSO- d_6) δ 8.23, 7.70, 7.50, 4.76, 4.17, 3.79, 3.42, 3.29, 2.64, 1.82, 1.78. Anal. Found: C, 50.58; H, 4.78; N, 16.36; S, 8.07.

Example 64. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(hydroxyimino)ethyl]-1,3,4-thiadiazol-2-

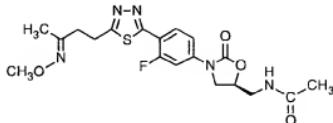
15 *yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = \text{CH}_3\text{CO}$, $R^2 = \text{HC}(\text{NOH})\text{CH}_2$). Refer to Scheme I.*



20 A mixture of stannous chloride (407 mg), thiophenol (462 mg), and triethylamine (0.98 mL) is prepared in CH_3CN (5 mL) at room temperature. The nitroethyl thiadiazole prepared in Example 53, Step 2 (585 mg) is added to this mixture as a solution in 5 mL of 1:1 MeOH and CH_2Cl_2 . The reaction is stirred for 2 hours and then concentrated to dryness. The residue is absorbed onto silica gel purified by flash chromatography using 5% MeOH in CH_2Cl_2 as eluent to afford 205 mg of the title compound.

Physical characteristics are as follows: mp 228-230 °C. ^1H NMR (DMSO- d_6) δ 8.25, 7.70, 7.55, 7.08, 4.80, 4.16, 3.79, 3.42, 1.81. Anal. Found: C, 48.51; H, 4.17; N, 17.39; S, 7.88.

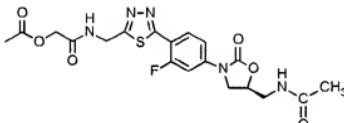
Example 65. (S)-N-[[3-[3-Fluoro-4-[5-[3-(methoxyimino)butyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = \text{CH}_3\text{CO}$, $R^2 = \text{CH}_3\text{C}(\text{NOCH}_3)\text{CH}_2\text{CH}_2$). Refer to Scheme I.



5 The ketone prepared in Example 16, Step 2 (200 mg) is dissolved in MeOH (2 mL) and H₂O (6 mL). To this solution is added methoxylamine hydrochloride (45 mg), Na₂CO₃ (28 mg), and one drop of acetic acid. The reaction is heated at 100 °C for 2 hours. The reaction is cooled and the solids are removed by filtration. The filtrate is flash chromatographed using 5% MeOH in CH₂Cl₂ as eluent to afford 104 mg of the title 10 compound.

Physical characteristics are as follows: mp 220-221 °C. ¹H NMR (DMSO-*d*₆) δ 8.26, 7.73, 7.55, 4.78, 4.19, 3.80, 3.73, 3.44, 3.33, 2.67, 1.85, 1.83. Anal. Found: C, 52.13; H, 5.03; N, 15.78; S, 7.20.

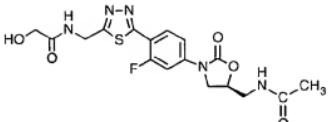
Example 66. (S)-N-[[[4-[5-[(Acetoxyacetyl)amino]methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = \text{CH}_3\text{CO}$, $R^2 = \text{CH}_3\text{CO}_2\text{CH}_2\text{C}(\text{O})\text{NHCH}_2$). Refer to Scheme I.



20 The amine prepared in Example 6, Step 2 (605 mg) is dissolved in CH₂Cl₂ (25 mL). To this solution is added acetoxyacetylchloride (348 μL) and pyridine (541 μL). The reaction is heated at reflux for 1 hour. The solvent is removed and the residue is absorbed onto silica gel and purified by flash chromatography using 5% MeOH in CH₂Cl₂ as eluent to afford 445 mg of the title compound.

Physical characteristics are as follows: mp 210-211 °C. ¹H NMR (DMSO-*d*₆) δ 9.00, 8.27, 7.74, 7.55, 4.75, 4.54, 4.20, 3.82, 3.44, 2.11, 1.84. Anal. Found: C, 48.41; H, 4.24; N, 14.63; S, 6.58.

Example 67. (S)-N-[5-[4-[5-[(Hydroxyacetylamo) methyl] 2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = \text{CH}_3\text{CO}$, $R^2 = \text{HOCH}_2\text{C}(\text{O})\text{NHCH}_3$). Refer to Scheme I.

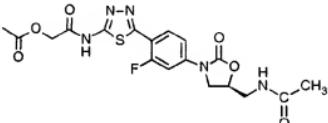


5

The thiadiazole prepared in Example 66 (250 mg) is suspended in MeOH (8 mL) at room temperature and K_2CO_3 (104 mg) is added. The reaction is stirred at room temperature for 30 minutes and then diluted with CH_2Cl_2 until homogeneous. The solids are removed by filtration and the reaction is concentrated. The residue is dissolved in MeOH and CH_2Cl_2 , absorbed onto silica gel and purified by flash chromatography using 8% MeOH in CH_2Cl_2 as eluent to afford 108 mg of the title compound.

Physical characteristics are as follows: mp 202-5 °C. ^1H NMR (DMSO- d_6) δ 8.80, 8.26, 7.73, 7.55, 5.26, 4.76, 4.19, 3.89, 3.82, 3.44, 1.84. Anal. Found: C, 47.76; H, 4.39; N, 15.97; S, 7.28.

15 Example 68. (S)-N-[5-[4-[5-[(Acetylamo) methyl] 2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]-2-(acetoxy)acetamide. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = \text{CH}_3\text{CO}$, $R^2 = \text{CH}_3\text{CO}_2\text{CH}_2\text{C}(\text{O})\text{NH}$). Refer to Scheme I.

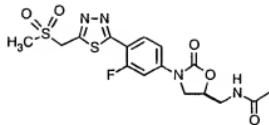


20 The aminothiadiazole prepared in Example 30 (100 mg) is dissolved in pyridine (5 mL) and chilled in an ice bath. Acetoxyacetyl chloride (184 μL) is added and the ice bath is removed. The reaction is stirred for 30 minutes and then concentrated in vacuo. The residue is dissolved in MeOH/ CH_2Cl_2 , absorbed onto silica gel, and flash chromatographed using 4% MeOH in CH_2Cl_2 as eluent to afford 89 mg of the title compound.

Physical characteristics are as follows: mp 245–246 °C. ^1H NMR (DMSO- d_6) δ 13.0, 8.26, 7.71, 7.55, 4.85, 4.78, 4.19, 3.82, 3.44, 2.14, 1.84. Anal. Found: C, 47.66; H, 4.14; N, 14.94; S, 6.74.

Example 69. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[(methylsulfonyl)methyl]-1,3,4-thiadiazol-2-yl]phenyl]methyl]sulfonyl]methane

5 yl[phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (I-A. $X^1 = F$, $X^2 = H$, $R^1 = CH_3CO$, $R^2 = CH_3SO_2CH_3$). Refer to Scheme I.

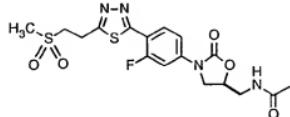


10 The sulfide prepared in Example 21, Step 2 (177 mg) is suspended in 1:1 methanol/water (4.0 mL) and oxone (359 mg) is added. The reaction mixture is heated at reflux for 2 hours and then cooled. The solid is isolated by filtration, washed with water and dried. The solid is dissolved in THF/acetone, absorbed onto silica gel and purified by flash chromatography using 5 % MeOH in CH_2Cl_2 as the eluent to afford 136 mg of the title compound.

Physical characteristics are as follows: mp 216-217 °C. ^1H NMR (DMSO-*d*₆) δ 8.32, 8.25, 7.74, 7.59, 5.32, 4.79, 4.20, 3.83, 3.45, 3.16, 1.84. Anal. Found: C, 44.68; H, 4.06; N, 12.95; S, 14.65.

Example 70. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylsulfonyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]methyl]sulfonyl]methane

20 $\text{y}] \text{phenyl}] \text{-2-oxo-5-oxazolidinyl}] \text{methyl}] \text{acetamide. (I-A. } \text{X}^1 = \text{F, } \text{X}^2 = \text{H, R} = \text{CH}_3\text{CO, R}^2 = \text{CH}_3\text{SO}_2\text{CH}_2\text{CH}_2\text{). Refer to Scheme I.}$

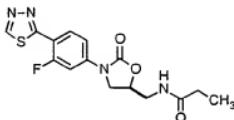


25 The sulfide prepared in Example 23, Step 2 (303 mg) is suspended in 1:1 methanol/water (8.0 mL). Oxone (590 mg) is added and the reaction mixture is heated at

reflux for 3 hours and then cooled. The solid is isolated by filtration, washed with water and dried. The solid is dissolved in THF/acetone, absorbed onto silica gel and purified by flash chromatography using 5 % MeOH in CH_2Cl_2 as the eluent to afford 213 mg of the title compound.

5 Physical characteristics are as follows: mp 217-218 °C. ^1H NMR (DMSO- d_6) δ 8.26, 7.76, 7.56, 4.78, 4.19, 3.81, 3.69, 3.63, 3.44, 3.08, 1.83. Anal. Found: C, 45.61; H, 4.41; N, 12.52; S, 14.32.

Example 71. (S)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CH}_2\text{CO}$, 10 $\text{R}^2 = \text{H}$). Refer to Scheme I.

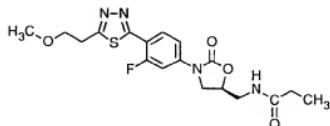


Step 1. The thiadiazole prepared in Example 9 (1.65 g) is dissolved in MeOH (130 mL) and 6M HCl (42 mL) is added. The reaction is heated at reflux for 24 hours and 15 then cooled and diluted with ether (20 mL). The precipitate is filtered, washed with ether and dried to afford 1.60 g of the aminomethyl oxazolidinone as an HCl salt.

Step 2. The aminomethyl oxazolidinone prepared in Step 1 (249 mg) is dissolved in THF (10 mL) and saturated, aqueous Na_2CO_3 (10 mL) is added. The solution is chilled in an ice bath and propionyl chloride (98 μL) is added. The ice bath is removed, and the 20 reaction is stirred for 1 hour. The liquid phases are separated and the aqueous phase is extracted with CH_2Cl_2 . The combined organic phases are diluted with MeOH (10 mL) in order to dissolve the suspended solids. This organic solution is dried with MgSO_4 , filtered, and concentrated. The residue is triturated with *t*-butyl methyl ether and a few drops of MeOH to afford a solid which is filtered and dried to give 234 mg of the title 25 compound.

Physical characteristics are as follows: mp 232-234 °C. ^1H NMR (DMSO- d_6) δ 9.70, 8.31, 8.17, 7.73, 7.54, 4.79, 4.18, 3.82, 3.44, 2.08, 0.93. Anal. Found: C, 50.77; H, 4.27; N, 15.75; S, 9.15.

Example 72. (S)-N-[[3-[3-Fluoro-4-[5-(2-methoxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CH₂CO, R² = CH₃OCH₂CH₂). Refer to Scheme I.



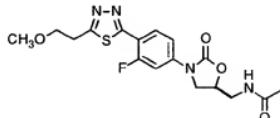
5 Step 1. The 2-chloroethyl thiadiazole prepared in Example 42 (760 mg) is dissolved in MeOH (60 mL) and 6M HCl (22 mL) is added. This solution is refluxed for 24 hours and then cooled and diluted with ether (20 mL). The precipitate is filtered, washed with ether and dried to afford 800 mg of the 2-methoxyethyl thiadiazole intermediate amine as an HCl salt.

10 Step 2. The amine salt prepared in step 1 (700 mg) is dissolved in a mixture of 15 mL of THF and 15 mL of saturated, aqueous Na₂CO₃ at 0 °C. Propionyl chloride (170 μ L) is added and the reaction mixture is stirred at room temperature for 3 hours. The reaction is concentrated and the residue is dissolved in MeOH and CH₂Cl₂ and absorbed onto silica gel. The product is purified by flash chromatography using 2.5% MeOH (saturated with NH₃) in CH₂Cl₂ as eluent to afford 175 mg of the title compound.

15 Physical characteristics are as follows: mp 189-190 °C. ¹H NMR (DMSO-*d*₆) δ 8.24, 8.16, 7.70, 7.52, 4.78, 4.16, 3.81, 3.69, 3.44, 3.37, 3.29, 2.08, 0.93. Anal. Found: C, 52.78; H, 5.21; N, 13.65; S, 7.78.

Example 73. (S)-N-[[3-[3-Fluoro-4-[5-(2-methoxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-

20 oxo-5-oxazolidinyl]methyl]acetamide. (I-A, X¹ = F, X² = H, R¹ = CH₃CO, R² = CH₃OCH₂CH₂). Refer to Scheme I.

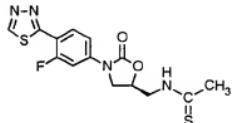


The amine salt prepared in Step 1 of Example 72 (150 mg) is dissolved in a mixture of THF (5 mL) and saturated, aqueous Na₂CO₃ (5 mL) at 0 °C. To this solution is added acetyl chloride (30 μ L), the reaction is allowed to warm to room temperature, and stirred for one hour. The reaction is diluted with water (5 mL) and extracted with

CH_2Cl_2 . The organic phases are combined, dried over MgSO_4 , filtered, and concentrated to give 142 mg of the title compound.

Physical characteristics are as follows: mp 187-188°C. ^1H NMR (DMSO- d_6) δ 8.26, 7.73, 7.53, 4.78, 4.20, 3.85, 3.71, 3.45, 3.40, 3.31, 1.84. Anal. Found: C, 51.43; H, 5.49; N, 13.95; S, 8.03.

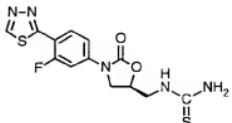
Example 74. (S)-N-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]ethanethioamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CS}$, $\text{R}^2 = \text{H}$). Refer to Scheme I.



10 The amine hydrochloride salt prepared in Step 1 of Example 71 (300 mg) is dissolved in THF (10 mL). Triethylamine (507 μL) and ethyldithioacetate (210 μL) are added to the solution. The reaction mixture is stirred at room temperature for 1.5 hours and then concentrated to dryness. The residue is taken up in CH_2Cl_2 and washed with 10% KHSO_4 solution, H_2O , and brine. The aqueous portions are back washed with 15 CH_2Cl_2 . The combined organic layers are dried over MgSO_4 , filtered and absorbed onto silica for purification by flash chromatography using 2.5% MeOH in CH_2Cl_2 as eluent to give 175 mg of the title compound.

Physical characteristics are as follows: mp 195-196 °C. ^1H NMR (DMSO- d_6) δ 10.4, 9.7, 8.31, 7.74, 7.56, 5.00, 4.23, 3.90, 2.43. Anal. Found: C, 47.53; H, 3.89; N, 15.70; S, 18.08.

Example 75. (S)-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]thiourea. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{H}_2\text{NCS}$, $\text{R}^2 = \text{H}$). Refer to Scheme I.



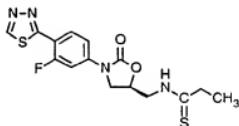
25 Step 1. The amine hydrochloride salt prepared in Step 1 of Example 71 (500 mg) is dissolved in 60 mL of CH_2Cl_2 . This solution is added at 0 °C to a stirred solution of

1,1'-thiocarbonyl-di-2-(1H)-pyridone (422 mg) in CH_2Cl_2 (18 mL). The reaction is warmed to room temperature and stirred overnight. Triethylamine (315 μL) is added and the reaction is stirred for an additional hour. The reaction is then washed with H_2O and brine and dried over Na_2SO_4 , filtered and concentrated. The residue is absorbed onto 5 silica and purified by flash chromatography using 20% CH_3CN in CH_2Cl_2 as eluent to give 250 mg of an isothiocyanate which is used immediately in the next reaction.

Step 2. The isothiocyanate (240 mg) prepared in Step 1 is dissolved in THF (20 mL) and the resulting solution cooled to 0 °C. Ammonia gas is bubbled into the reaction for 6 minutes. The reaction is capped and allowed to stand for 45 minutes. The reaction is 10 then concentrated and triturated with Et_2O and a few drops of MeOH to give 230 mg of the title compound.

Physical characteristics are as follows: mp 215-217 °C. ^1H NMR (DMSO- d_6) δ 9.85, 8.31, 7.93, 7.74, 7.55, 7.20, 4.90, 4.20, 3.85. Anal. Found: C, 43.91; H, 3.59; N, 19.40; S, 17.92.

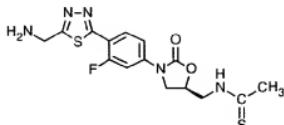
15 Example 76. (S)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanethioamide. (I-A, $\text{X}^1 = \text{F}$, $\text{X}^2 = \text{H}$, $\text{R}^1 = \text{CH}_3\text{CH}_2\text{CS}$, $\text{R}^2 = \text{H}$). Refer to Scheme I.



The thiadiazole propionamide prepared in Example 71, Step 2 (238 mg) is dissolved in 1,4-dioxane (7 mL) and Lawesson's reagent (286 mg) is added to this solution. The reaction is heated at 100 °C for 18 hours. The dioxane is removed in vacuo and the residue is dissolved in MeOH and CH_2Cl_2 , absorbed onto silica gel, and purified by flash chromatography using 5% MeOH in CH_2Cl_2 as eluent to give 225 mg of the title compound.

25 Physical characteristics are as follows: mp 179-181 °C. ^1H NMR (DMSO- d_6) δ 10.3, 9.80, 8.31, 7.73, 7.55, 5.02, 4.23, 3.92, 2.58, 1.13. Anal. Found: C, 48.94; H, 4.36; N, 14.84; S, 17.21.

Example 77. *N*-(*[(5S)-3-[(4-[5-(aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl]ethanethioamido*). (I-A, $X^1 = F$, $X^2 = H$, $R^1 = CH_3CS$, $R^2 = H_2NCH_2$). Refer to Scheme I.



5

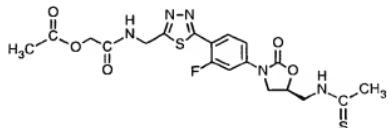
Step 1. The FMOC-protected amine prepared in Example 6, Step 1 (3.0 g) is dissolved in 60 mL of p-dioxane at room temperature. Lawesson's reagent (2.13 g) is added and the reaction is heated at 100 °C for 2 hours. The reaction is cooled to room 10 temperature and diluted with Et₂O. The resulting precipitate is triturated with MeOH to give 2.6 g of the thioamide.

Step 2. The thioamide prepared in Step 1 (2.4 g) is stirred in 41 mL of piperidine at room temperature for 30 minutes. The reaction mixture is then concentrated.

Purification by flash chromatography using 10% MeOH in CH₂Cl₂ as eluent gives 1.17 g 15 of the title compound.

Physical characteristics are as follows: mp 205-206 °C. ¹H NMR (DMSO-d6) δ 10.35, 8.25, 7.73, 7.55, 5.00, 4.24, 4.16, 3.90, 2.58, 2.50. Anal. Found: C, 47.12; H, 4.26; N, 18.16; S, 16.48.

Example 78. *2-[(5-[4-((5S)-5-[(ethanethioylamino)methyl]-2-oxo-1,3-oxazolidin-3-yl]-2-fluorophenyl)-1,3,4-thiadiazol-2-yl)methyl]amino)-2-oxoethyl acetate*. (I-A, $X^1 = F$, $X^2 = H$, $R^1 = CH_3CS$, $R^2 = CH_3CO_2CH_2CONHCH_2$). Refer to Scheme I.



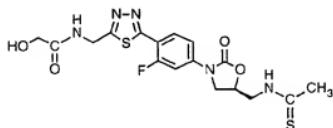
25 The amine prepared in Example 77, Step 2 (850 mg) is stirred in 35 mL of CH₂Cl₂. To this is added acetoxyacetylchloride (480 μL) and pyridine (730 μL). The reaction is heated to reflux for 1 hour. The reaction is cooled to room temperature and concentrated. Purification by flash chromatography using 1% NH₄OH, 10% isopropanol,

and 89 % CHCl_3 as eluent results in partial hydrolysis of the acetoxyacetamide and gives a mixture of compounds. Further purification of this mixture by flash chromatography using 5% MeOH in CHCl_3 as eluent affords 157 mg of the title compound.

Physical characteristics are as follows: mp 145-146 °C. ^1H NMR (DMSO- d_6) δ 5 10.35, 9.00, 8.28, 7.74, 7.54, 5.00, 4.75, 4.55, 4.25, 3.94, 2.50, 2.11. Anal. Found: C, 47.18; H, 4.28; N, 14.21; S, 12.2.

Example 79. N -[5-(4-[(5S)-5-[(ethanethioylamino)methyl]-2-oxo-1,3-oxazolidin-3-yl]-2-fluorophenyl)-1,3,4-thiadiazol-2-yl]methyl]-2-hydroxyacetamide. (I-A, X^1 = F, X^2 = H, R^1 = CH_3CS , R^2 = $\text{HOCH}_2\text{CONHCH}_2$). Refer to Scheme I.

10



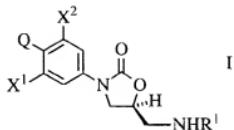
The mixture produced in the first chromatography of Example 78 is further purified by flash chromatography using 5% MeOH in CHCl_3 to afford 319 mg of the title compound.

Physical characteristics are as follows: mp 182-184 °C. ^1H NMR (DMSO- d_6) δ 10.40, 8.80, 8.27, 7.73, 7.57, 5.62, 5.00, 4.74, 4.24, 3.90, 2.50. Anal. Found: C, 46.28; H, 4.15; N, 15.88; S, 14.31.

20

CLAIMS

1. A compound of formula I:

wherein R¹ is

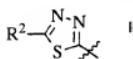
- 5 (a) -COR³,
- (b) -COCH₂Cl,
- (c) -COCHCl₂,
- (d) -COCH₂F,
- (e) -COCHF₂,
- 10 (f) -CO₂CH₃,
- (g) -SO₂CH₃,
- (h) -COCH₂OH,
- (i) -CSR³,
- (j) -CSNH₂, or
- 15 (k) -CSNHCH₃;

wherein X¹ and X² are independently

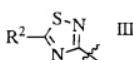
- (a) H,
- (b) F, or
- (c) Cl;

20 wherein Q is

- (a) 1,3,4-thiadiazol-2-yl:

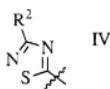


- (b) 1,2,4-thiadiazol-3-yl:



25

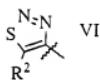
(c) 1,2,4-thiadiazol-5-yl:



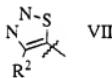
(d) 1,2,5-thiadiazol-3-yl:



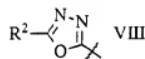
(e) 1,2,3-thiadiazol-4-yl:



10 (f) 1,2,3-thiadiazol-5-yl:

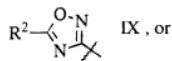


(g) 1,3,4-oxadiazol-2-yl:

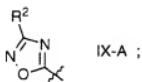


15

(h) 1,2,4-oxadiazol-3-yl:



(i) 1,2,4-oxadiazol-5-yl



wherein R^2 is

- (a) R^3- ,
- (b) $R^4CO_3(CH_2)_n-$,
- 5 (c) $NC(CH_2)_n-$,
- (d) $R^3OCO(CH_2)_n-$,
- (e) $R^3R^5NCO(CH_2)_n-$,
- (f) $R^3R^5N(CH_2)_n-$,
- (g) $R^4CONR^5(CH_2)_n-$,
- 10 (h) $CF_3(CH_2)_n-$,
- (i) $CF_2H(CH_2)_n-$,
- (j) $R^4CO(CH_2)_n-$,
- (k) $F(CH_2)_n-$,
- (l) $Cl(CH_2)_n-$,
- 15 (m) $Br(CH_2)_n-$,
- (n) $R^3O(CH_2)_n-$,
- (o) $R^3S(CH_2)_n-$,
- (p) $R^3SO(CH_2)_n-$,
- (q) $R^3SO_2(CH_2)_n-$,
- 20 (r) $R^3SO_2NR^5(CH_2)_n-$,
- (s) $R^3R^4C(OH)(CH_2)_n-$,
- (t) $R^3R^4C(NHR^5)(CH_2)_n-$,
- (u) $HO_2C(CH_2)_n-$,
- (v) $O_2N(CH_2)_n-$,
- 25 (w) C_2-C_6 alkenyl,
- (x) C_2-C_6 alkynyl,
- (y) $-CCl_3$,
- (z) $R^3ON=CR^3(CH_2)_n-$,
- (aa) $NCNR^5(CH_2)_n-$,
- 30 (bb) $R^3ONR^5(CH_2)_n-$, or
- (cc) $R^3OC(O)NR^5(CH_2)_n-$;

wherein n is 0, 1, 2, 3, 4 or 5;

wherein p is 1, 2 or 3;

wherein R^3 is

- (a) H,
- (b) C_1 - C_5 alkyl, or
- (c) cyclopropyl;

5 wherein R^4 is

- (a) H,
- (b) C_1 - C_5 alkyl-,
- (c) cyclopropyl-,
- (d) $R^3O(CH_2)_p$ -, or
- (e) $R^3CO_2(CH_2)_p$;

10 wherein R^5 is

- (a) H, or
- (b) C_1 - C_3 alkyl;

or a pharmaceutically acceptable salt thereof;

15 with the following proviso:

at least one of X^1 and X^2 is F or Cl.

2. The compound of claim 1

wherein R^1 is

20 (a) -COR³, or
 (b) -CSR³;

wherein X^1 and X^2 are independently

- (a) H, or
- (b) F;

25 wherein Q is the moiety of formula II or IV;

wherein R^2 is

- (a) R^3 ,
- (b) $R^3CO_2(CH_2)_n$ -,
- (c) $NC(CH_2)_n$ -,
- (d) $R^3OCO(CH_2)_n$ -,
- (e) $R^3R^5NCO(CH_2)_n$ -,
- (f) $R^3R^5N(CH_2)_n$ -,
- (g) $R^4CONR^5(CH_2)_n$ -,

- (h) $\text{CF}_3(\text{CH}_2)_n^-$,
- (i) $\text{R}^4\text{CO}(\text{CH}_2)_n^-$,
- (j) $\text{F}(\text{CH}_2)_n^-$,
- (k) $\text{Cl}(\text{CH}_2)_n^-$,
- 5 (l) $\text{R}^3\text{O}(\text{CH}_2)_n^-$,
- (m) $\text{R}^3\text{S}(\text{CH}_2)_n^-$,
- (n) $\text{R}^3\text{SO}(\text{CH}_2)_n^-$,
- (o) $\text{R}^3\text{SO}_2(\text{CH}_2)_n^-$,
- (p) $\text{R}^3\text{SO}_2\text{NR}^5(\text{CH}_2)_n^-$,
- 10 (q) $\text{O}_2\text{N}(\text{CH}_2)_n^-$, or
- (r) $\text{R}^3\text{R}^4\text{C}(\text{NHR}^5)(\text{CH}_2)_n^-$;
- (o) $\text{R}^3\text{SO}_2\text{NR}^3(\text{CH}_2)_n^-$,
- (p) $\text{R}^3\text{R}^4\text{C}(\text{OH})(\text{CH}_2)_n^-$, or
- (q) $\text{C}_2\text{-C}_6$ alkenyl;

15 wherein n is 0, 1, or 2;

wherein R^4 is

- (a) H,
- (b) $\text{C}_1\text{-C}_3$ alkyl, or
- (c) cyclopropyl.

20

3. The compound of claim 2

wherein R^2 is

- (a) R^3 ,
- (b) $\text{NC}(\text{CH}_2)_n^-$,
- (c) $\text{R}^3\text{NHCO}(\text{CH}_2)_n^-$,
- (d) $\text{R}^4\text{CO}(\text{CH}_2)_n^-$,
- (e) $\text{F}(\text{CH}_2)_n^-$,
- (g) $\text{Cl}(\text{CH}_2)_n^-$,
- (h) $\text{R}^3\text{O}(\text{CH}_2)_n^-$,
- 25 (i) $\text{R}^3\text{S}(\text{CH}_2)_n^-$,
- (j) $\text{R}^3\text{NH}(\text{CH}_2)_n^-$, or
- (k) $\text{R}^4\text{CONH}(\text{CH}_2)_n^-$.

4. The compound of claim 3 wherein Q is the moiety of formula II.
5. The compound of claim 1 selected from the group consisting of:
 1. (*S*)-*N*-[[3-[4-(5-Cyano-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 2. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-carboxamide;
 3. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 - 10 4. (*S*)-*N*-[[3-[4-(5-Ethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 5. (*S*)-*N*-[[3-[3-Fluoro-4-(5-propyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 6. (*S*)-*N*-[[3-[4-[5-(Aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 - 15 7. *S*-*N*-[[3-[3-Fluoro-4-[5-[(methylsulfonyl)amino]methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 8. (*S*)-*N*-[[3-[3-Fluoro-4-(5-fluoromethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 - 20 9. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 10. (*S*)-*N*-[[3-[4-(5-Acetoxymethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 11. (*S*)-*N*-[[3-[3-Fluoro-4-(5-hydroxymethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 - 25 12. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methoxymethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 13. (*S*)-*N*-[[3-[4-[5-(Cyanomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
 - 30 14. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-acetamide;
 15. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

16. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-oxobutyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
17. (*SS*)-*N*-[[3-[3-Fluoro-4-[5-(3-hydroxybutyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 5 18. (*S*)-Methyl 5-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-propanoate;
19. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-propanamide;
20. (*S*)-*N*-[[3-[4-[5-(2-Cyanoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 10 21. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[(methylthio)methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
22. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[(methylsulfinyl)methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 15 23. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylthio)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
24. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylsulfinyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
25. (*S*)-Ethyl 5-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-acetate;
- 20 26. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(2-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
27. (*S*)-Ethyl 5-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-carboxylate;
- 25 28. (*SS*)-*N*-[[3-[3-Fluoro-4-[5-(2-hydroxypropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
29. (*S*)-*N*-[[3-[4-(4,5-Dihydro-5-oxo-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
30. (*S*)-*N*-[[3-[4-(5-Amino-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
31. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylthio)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

32. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

33. (*S*)-3-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,2,4-thiadiazole-5-carboxamide;

5 34. (*S*)-*N*-[[3-[3-Fluoro-4-(1,2,4-thiadiazol-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

35. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

10 36. (*S*)-*N*-[[3-[3-Fluoro-4-(1,2,4-oxadiazol-3-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

37. (*S*)-3-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,2,4-oxadiazole-5-carboxamide;

38. (*S*)-*N*-[[3-[4-(5-Cyano-1,2,4-oxadiazol-3-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

15 39. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

40. (*S*)-*N*-[[3-[3-Fluoro-4-(1,2,4-oxadiazol-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

41. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(formylamino)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

20 42. (*S*)-*N*-[[3-[4-[5-(2-Chloroethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

43. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(1-propenyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

25 44. (*S*)-*N*-[[3-[4-[5-(2-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

45. (*S*)-*N*-[[3-[4-[5-[2-(Acetylamino)ethyl]-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

46. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-[(methylsulfonyl)amino]ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

30 47. (*SS*)-*N*-[[3-[3-Fluoro-4-[5-(methylsulfinyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

48. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(1-methylethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

49. (*S*)-*N*-[[5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide;

50. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-hydroxypropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

51. [*S*-(*R*^{*,*R*^{*})-*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

52. [*S*-(*R*^{*,*S*^{*})-*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

53. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(2-nitroethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

54. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-nitropropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

55. [*S*-(*R*^{*,*R*^{*})-*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

56. [*S*-(*R*^{*,*S*^{*})-*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

57. (*S*)-*N*-[[3-[4-[5-(3-Aminopropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

58. (*S*)-*N*-[3-[5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]propyl]acetamide;

59. (*S*)-*N*-[[3-[4-(5-Acetyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

60. (*S*)-*N*-[[3-[4-[5-(3-Chloropropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

61. (*S*)-*N*-[[3-[4-[5-(3-Cyanopropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

62. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylsulfonyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

63. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-hydroxyimino)butyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

64. (S)-N-[[3-[3-Fluoro-4-[5-[2-(hydroxyimino)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

65. (S)-N-[[3-[3-Fluoro-4-[5-[3-(methoxyimino)butyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

5 66. (S)-N-[[5-[4-[5-[(Acetoxyacetyl)amino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide;

67. (S)-N-[[5-[4-[5-[(Hydroxyacetyl)amino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazol-2-yl]methyl]acetamide;

68. (S)-N-[5-[4-[5-[(Acetyl)amino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-10 1,3,4-thiadiazol-2-yl]-2-(acetoxy)acetamide;

69. (S)-N-[[3-[3-Fluoro-4-[5-[methylsulfonyl)methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

70. (S)-N-[[3-[3-Fluoro-4-[5-[2-(methylsulfonyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

15 71. (S)-N-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

72. (S)-N-[[3-[3-Fluoro-4-[5-(2-methoxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

73. (S)-N-[[3-[3-Fluoro-4-[5-(2-methoxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

20 74. (S)-N-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]ethanethioamide;

75. (S)-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]thiourea;

25 76. (S)-N-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanethioamide;

77. N-[(5S)-3-[4-[5-(aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl]ethanethioamide;

78. 2-((5S)-5-[(ethanethioyl)amino)methyl]-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl)-1,3,4-thiadiazol-2-yl]methyl]amino)-2-oxoethyl acetate; and

30 79. N-[(5-((4-((5S)-5-[(ethanethioyl)amino)methyl]-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl)-1,3,4-thiadiazol-2-yl)methyl]-2-hydroxyacetamide.

6. The compound of claim 5 which is
1. (*S*)-*N*-[[3-[4-(5-Cyano-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
2. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 5 3. (*S*)-*N*-[[3-[4-(5-Ethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
4. (*S*)-*N*-[[3-[4-[5-(Aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 10 5. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[(methylsulfonyl)amino]methyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
6. (*S*)-*N*-[[3-[3-Fluoro-4-(5-fluoromethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
7. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 15 8. (*S*)-*N*-[[3-[4-(5-Acetoxymethyl-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
9. (*S*)-*N*-[[3-[3-Fluoro-4-(5-hydroxymethyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 20 10. (*S*)-*N*-[[3-[4-[5-(Cyanomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
11. (*S*)-5-[4-[5-[(Acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1,3,4-thiadiazole-2-acetamide;
12. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-oxobutyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 25 13. (*S*)-*N*-[[3-[4-[5-(2-Cyanoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
14. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylsulfinyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
- 30 15. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(2-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;
16. (*S*)-*N*-[[3-[4-(4,5-Dihydro-5-oxo-1,3,4-thiadiazol-2-yl)-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

17. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(methylthio)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

18. (*S*)-*N*-[[3-[3-Fluoro-4-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

5 19. (*SS*)-*N*-[[3-[3-Fluoro-4-[5-(methylsulfinyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

20. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-hydroxypropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

21. [*S*-(*R*^{*,*R*^{*})]-*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide}

10 22. [*S*-(*R*^{*,*S*^{*})]-*N*-[[3-[3-Fluoro-4-[5-(1-hydroxyethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

23. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(2-nitroethyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

15 24. (*S*)-*N*-[[3-[3-Fluoro-4-[5-(3-nitropropyl)-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

25. [*S*-(*R*^{*,*R*^{*})]-*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

20 26. [*S*-(*R*^{*,*S*^{*})]-*N*-[[3-[4-[5-(1-Aminoethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;}

27. (*S*)-*N*-[[3-[4-[5-(3-Cyanopropyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

28. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[3-(hydroxyimino)butyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

25 29. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(hydroxyimino)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

30. (*S*)-*N*-[[3-[3-Fluoro-4-[5-[2-(methylsulfonyl)ethyl]-1,3,4-thiadiazol-2-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide;

31. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanamide;

30 32. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]ethanethioamide;

33. (*S*)-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]thiourea;

34. (*S*)-*N*-[[3-[3-Fluoro-4-(1,3,4-thiadiazol-2-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl]propanethioamide;

5 35. *N*-[((5*S*)-3-{4-[5-(aminomethyl)-1,3,4-thiadiazol-2-yl]-3-fluorophenyl}-2-oxa-1,3-oxazolidin-5-yl)methyl]ethanethioamide;

36. 2-((5-(4-((5*S*)-5-[(ethanethioylamino)methyl]-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl)-1,3,4-thiadiazol-2-yl)methyl)amino)-2-oxoethyl acetate; or

37. *N*-{(5-(4-((5*S*)-5-[(ethanethioylamino)methyl]-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl)-1,3,4-thiadiazol-2-yl)methyl}-2-hydroxyacetamide.

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INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/US 98/13437A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D417/10 C07D413/10 A61K31/42

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 09328 A (PHARMACIA & UPJOHN COMPANY) 13 March 1997 see claims; examples 87,88 ---	1-4
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 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

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"X" document of particular relevance; the claimed invention cannot be made without combining the document to be examined to involve an inventive step when the document is read alone

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"*&" document member of the same patent family

Date of the actual completion of the international search

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Name and mailing address of the ISA
European Patent Office, P.B. 5816 Patenttaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Henry, J

INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/US 98/13437

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat'l Application No
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